

CASE REPORT

MULTIMODAL TREATMENT FOR METASTATIC BREAST CANCER

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SUMMARY

Background: The prognosis for patients with metastatic breast cancer has significantly improved over the past decade due to advances in treatment. Patients who present with large primary tumors and extensive local disease are at high risk for both distant and loco-regional disease recurrence. Here we evaluate the local response to external beam radiotherapy for stage IV breast cancer.

Case report: We present the case of a 65 year old female, diagnosed with stage IV invasive left-breast ductal carcinoma, biopsied in 2013, clinical staging T3N2M1, with lung metastasis and skin metastasis localized at the left breast. The histopathological finding after the tumor biopsy was invasive mammary carcinoma, moderately differentiated. Following multiple chemotherapy series and Trastuzumab treatment, at the evaluation computed tomography (CT)-scans, the patient shows mixed response with partial tumoral and systemic response with the apparition of skin metastasis on the same breast. At post chemotherapy evaluation, an 8 centimeter ulcerative skin metastasis is reviewed. Because surgery was not feasible, left breast palliative radiotherapy was taken into consideration.

Conclusions: This patient, suffering from progressive systemic disease with localized symptomatology benefits because this treatment reduces discomfort greatly and improves quality of life, taking into consideration the low life expectancy. Radiotherapy is suitable as an adequate treatment to achieve good local control.

Key words: breast cancer, metastasis, radiotherapy

RÉSUMÉ

Traitement multiple pour le cancer métastatique du sein

Introduction: Le pronostic pour les patients atteints de cancer métastatique du sein s'est considérablement amélioré au cours de la dernière décennie en raison du progrès dans le traitement. Les patients qui se présentent avec de grosses tumeurs primaires ou une maladie étendue locale sont à haut risque de récurrence de la maladie à la fois à distance et loco-régionale. Ici, nous évaluons la réponse locale à la radiothérapie externe pour un cancer du sein de stade IV.

Matériel et méthode: Nous présentons le cas d'une femme de 65 ans, diagnostiquée avec carcinome canalaire gauche invasif du sein en stade IV, stade clinique T3N2M1, aux métastases pulmonaires et de la peau localisées au sein gauche. Le résultat histo-pathologique après la biopsie de la tumeur a été carcinome mammaire invasif, modérément différencié. Après la série de la chimio-thérapie et le traitement multiple avec du trastuzumab, à la tomographie computerisée le patient a présenté une réaction mitigée tumorale partielle et systémique avec l'apparition de métastases de la peau sur le même sein. A l'évaluation post-chimiothérapie on a examiné une métastase de la peau ulcéreuse de 8 cm. Vu que l'opération n'a pas été possible, on a pris en considération la radiothérapie palliative du sein gauche.

Conclusions: Ce patient, souffrant d'une maladie systémique progressive à symptomatologie localisée a des bénéfices parce que ce traitement réduit la malaise et améliore la qualité de la vie considérant la faible attente de vie. La radiothérapie est appropriée en tant que traitement adéquat afin d'obtenir un bon contrôle local.

Mots clés: cancer du sein, métastases, radiothérapie

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INTRODUCTION

Metastatic breast cancer remains a treatable but still generally incurable disease. The most notable research advances are the ones regarding the radiation treatment planning and targeted therapies, most notably the human epidermal growth factor receptor (HER) - 2 positive subtypes. The purpose of care is to increase life expectancy and improve quality of life, but regardless of the advances, median overall survival of patients with metastatic breast cancer is still only 2–3 years [1-5].

The role of radiotherapy in the treatment of breast cancer has a long and controversial history [6], but with the introduction of new techniques and precise linear accelerators, it has become an important one for all stages of breast cancer. While its use as adjuvant therapy in patients undergoing mastectomy for stages I and II disease is becoming the standard, it has also developed into an essential constituent of the combined modality approach for stages III and IV disease. [7]

CASE REPORT

We report the case of a 65-year-old female, diagnosed in 2005 with stage IIIA, invasive right-breast ductal cancer. Lumpectomy was performed, and then the patient underwent six cycles of chemotherapy with Cyclophosphamide Methotrexate Fluorouracil (CMF), breast and axillary irradiation and hormone therapy. In 2007 she is diagnosed with thyroid neoplasm, operated, underwent radioactive iodine treatment and is currently under hormone replacement therapy.

In 2013, the patient was diagnosed with stage IV invasive left-breast ductal carcinoma, biopsied, clinical staging T3N2M1 PUL, M1 SKY localized at the left breast. The histopathological and immunohistochemistry findings after the tumor biopsy were invasive mammary ductal carcinoma, G2 with molecular profile of HER 2 (human epidermal growth factor receptor 2) 3+, negative estrogen

receptor (ER), negative progesterone receptor (PGR), Ki 67 70%.

First line of treatment consisted in Epirubicin, Cyclophosphamide and 5-Fluorouracil with no response. After three cycles, Docetaxel and Trastuzumab chemotherapy was started, and the patient showed tumor shrinkage and partial response to lung metastasis. After several cycles of Docetaxel and Trastuzumab, the patient presented skin metastasis on the same breast. Chemotherapy was changed again and the patient received further lines of chemotherapy with Vinorelbine and Capecitabine concurrent with Trastuzumab with response to lung metastases and mixed response to skin lesions.

The CT-scan at the presentation, describes at the left breast, a 27 mm isodense nodule, iodophile, irregular shape, left axillaries adenopathies 7-15 mm, basal right pulmonary isodense nodule 13 mm, unique. One-year after chemotherapy, the CT scan highlights at the left breast, a 21 mm nodule, left axillaries adenopathies, basal right pulmonary, 8 mm isodense nodule.

Clinically after chemotherapy, an 8 cm ulcerative skin metastasis is reviewed. Because surgery was not feasible, left breast palliative radiotherapy was considered in case of oligometastatic disease. The patient underwent external beam radiotherapy (EBRT) to a total dose of 50 gray (Gy) to the planning target volume (PTV), which included left breast to the chest wall, local lymph nodes and skin metastasis, 200 centigram (cGy) per fraction, one fraction per day followed by a 10 Gy electron radiotherapy boost, 200 cGy per fraction, one fraction per day, to the skin metastasis. Written informed consent was obtained from the patient.

After completing EBRT, the clinical exam showed good local response. Control CT-scan shows 18 mm left breast nodule, few left axillaries adenopathies, ranging from 3 to 15 mm, and small right lung nodule. Clinically, the skin metastases measured 7 cm.

Progression free survival is 8 months with Docetaxel and Trastuzumab and the patient is still alive after 27 months since the stage IV left breast ductal carcinoma was diagnosed.

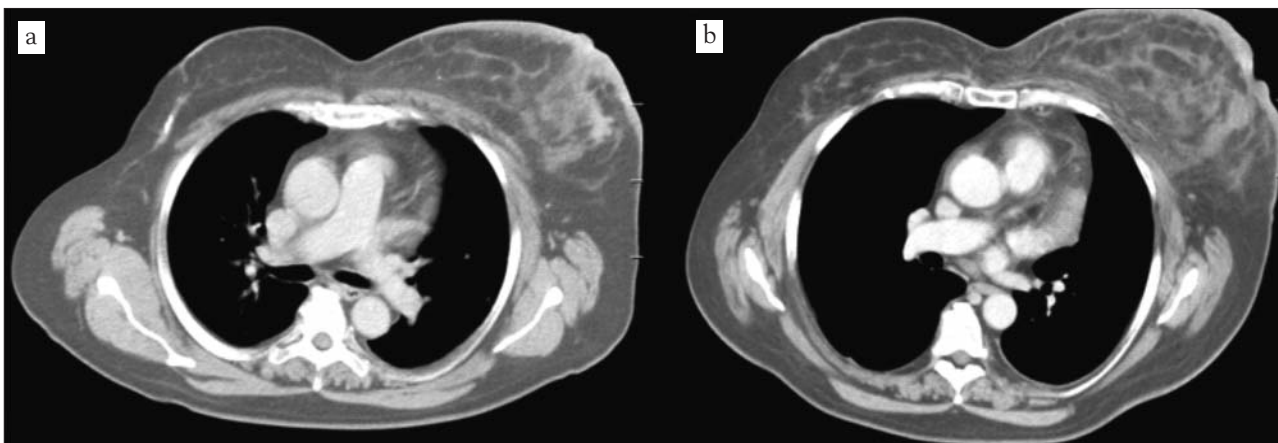


Figure 1- Thoracic transverse CT scans featuring the left breast in (a) June 2014, then in (b) July 2015

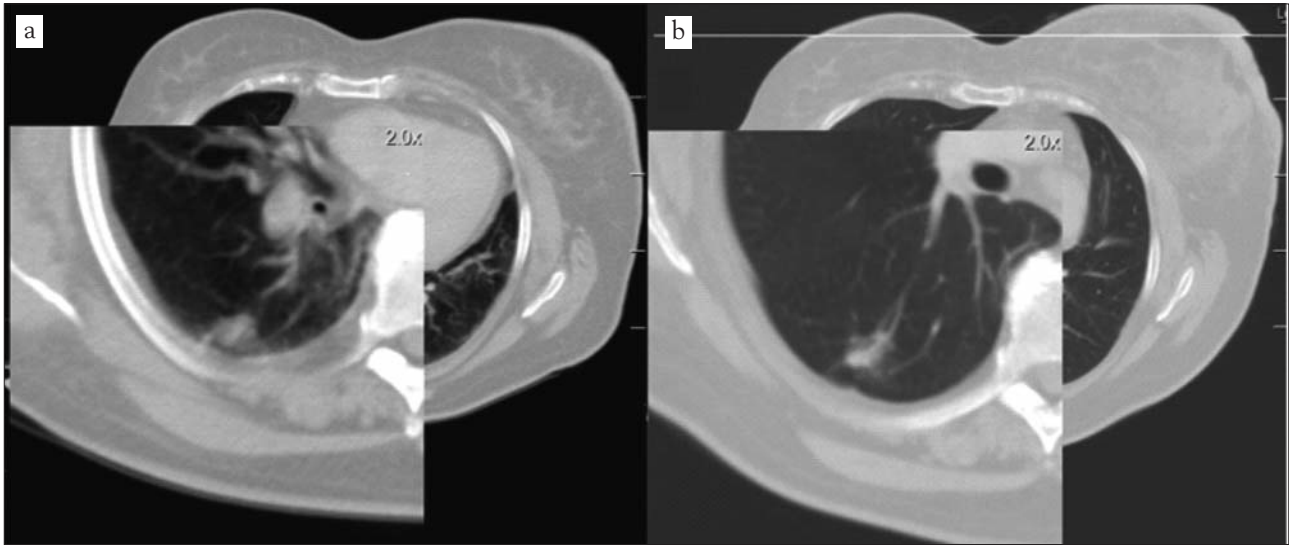


Figure 2 - Transverse CT scans featuring the lung metastasis in (a) June 2014, then in (b) July 2015

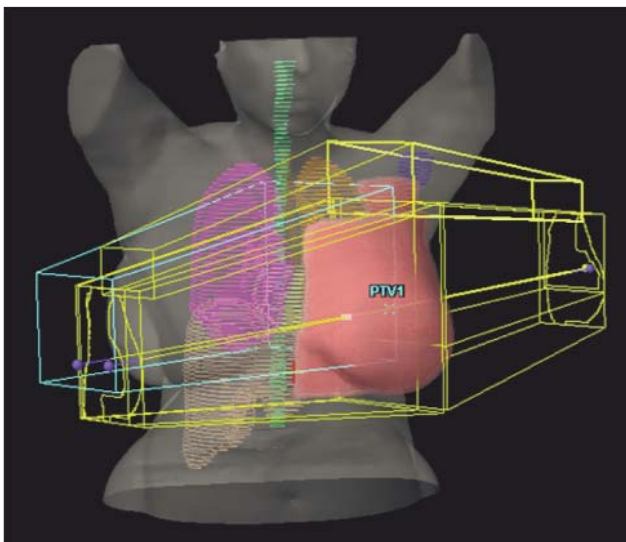


Figure 3- 3D reconstruction of the radiotherapy treatment plan

DISCUSSION

In the past decades, a case of metastatic breast cancer automatically came with a poor prognosis and few treatment options. This picture has changed dramatically, with the apparition of many therapies and also a shift in the mindset of how the disease is viewed by oncologists.

The term oligometastases, which is used to describe a limited number of metastases (3-4 clinically detectable metastases), was introduced in 1995 by Hellmann and Weichselbaum. It is a hypothesis as a clinical state in which the full metastatic potential is not reached and local therapy may offer cure in some patients [8].

Radiotherapy in metastatic cancers has evolved from palliative care to a potentially curative goal for localized oligometastases. Thereby, improving the local control of metastatic lesions with the use of 3D conformal radio-

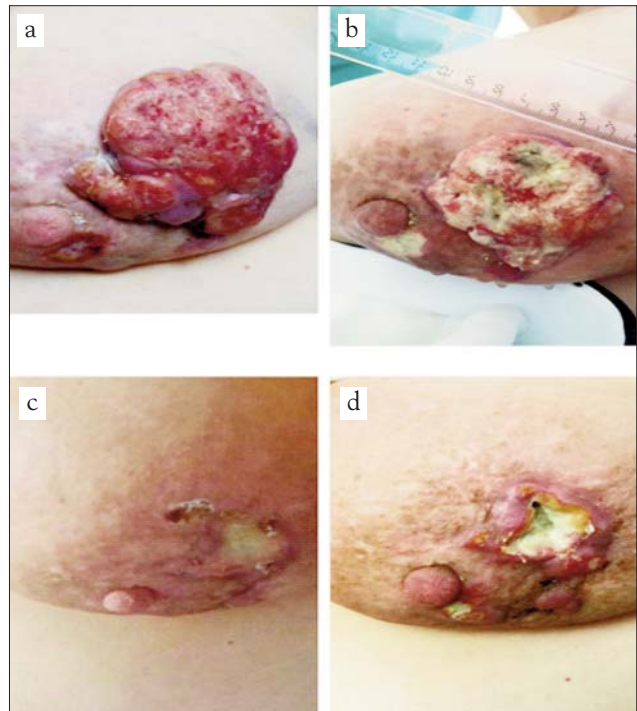


Figure 4 - Skin metastasis: (a) prior to radiation therapy, (b) after ten fractions of radiation therapy, (c) at the completion of radiation therapy and (d) two months after completion of radiation therapy

therapy is a promising approach for the patient with oligometastatic breast cancer.

In recent times, however, the use of radiotherapy including stereotactic radiotherapy offers a less invasive approach and might provide a potentially curative treatment of oligometastases [9,10]. A retrospective study had shown that the addition of locoregional treatment to systemic therapy improved survival in patient with advanced locoregional disease and metastases at diagnosis. This study found that radiotherapy as locoregional treatment was

effective in combination with surgery and also if administered exclusively without surgery [11]. Further studies are needed to evaluate the effectiveness of newer methods of radiotherapy as curative-intent local therapy in patients with oligometastases.

Surgical resection might become the solution of curative treatment in patients with single metastasis of breast cancer [12]. About 10–25% of patients with metastatic breast cancer develop lung metastases. [13,14]. The study Greenberg et al. [15], performed on 1,581 patients treated with combination chemotherapy for metastatic breast cancer, including 697 patients with lung metastases, showed the 5-year disease-free survival rate of only 2.4%. There are also studies in which surgery is taken into consideration regarding patients with a solitary pulmonary metastasis, and complete versus incomplete metastasectomy predicted better outcome [16]. However, this is not the case of solitary pulmonary metastasis, but lung metastasectomy might become the treatment of choice if local control is achieved.

Additionally, there is evidence suggesting the benefit use of Trastuzumab with chemotherapy, in women with advanced HER-2positive breast cancer, with Trastuzumab reserved for the time of disease progression on an initial chemotherapy regimen. Based on these results, trastuzumab is active and well tolerated as first-line treatment of women with metastatic breast cancer with HER2 3+ overexpression by immunohistochemistry (IHC) or gene amplification by fluorescence in situ hybridization (FISH) [17]. However, the question of optimal duration of trastuzumab therapy remains unresolved. Different metastases may have a different response to chemotherapy and targeted therapy. Skin metastases may have a vast response to systemic therapy compared to other types of metastases. We report a case of contralateral breast cancer, lung and skin metastasis in a patient with breast cancer after a disease-free interval of more than 8 years. Taking into consideration that there is a very limited number of patients, including cases with long disease-free intervals and solitary metastases, one of the remaining questions is if the local surgical approach is the treatment of choice in the case of a stage IV breast cancer; however, further analyses of a large number of cases are warranted to evaluate the clinical significance of this approach.

CONCLUSIONS

There is a strong need for close follow-up in patients with breast cancer because the incidence to develop the second primary cancer/metastases in contralateral breast is increased even after a long period of time.

In patients with oligometastatic diseases, systemic treatment (chemotherapy and targeted therapy) concurrently with local treatment consisting in radiotherapy can ameliorate the symptoms and may lead to good outcome and

quality of life. Personalized approach emphasizes the importance of multimodal treatment in this subset of patients.

Acknowledgement

This work received financial support through the project entitled "CERO – Career profile: Romanian Researcher", grant number POSDRU/159/1.5/S/135760, cofinanced by the European Social Fund for Sectoral Operational Programme Human Resources Development 2007-2013.

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