



# Survival in triple negative metastatic breast carcinoma

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**Keywords:** Breast Cancer, Metastases, Hormone Therapy, Immunohistochemistry

## Abstract

Breast cancer is the most common non-skin malignancy in women, the second most common cause of cancer death, and the main cause of death in women ages 45 to 55 years. An estimated 1 million cases of breast cancer are diagnosed annually worldwide. Approximately 5-10% of patients with breast cancer have distant metastases at first presentation.

The patient came to the Clinic of oncology and radiotherapy in March 2005 for further treatment with the diagnosis: *Carcinoma metastaticum vertebrae lumbosacralis*.

Initial treatment was included 6 cycles of chemotherapy, bisphosphonate therapy and realized radiotherapy. Tumor markers at the end of treatment: CEA 238; CA15-3: 19.6. After that a radical mastectomy of the left breast with dissection of left axilla was conducted and pathological analysis showed poorly differentiated ductal invasive carcinoma (grade 3 according to Nottingham Histologic Score) with immunohistochemistry findings: HER: negative, ER: negative, PR: negative or Triple negative breast cancer (TNBC).

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## Introduction

Breast cancer is the most common non-skin malignancy in women, the second most common cause of cancer death, and the main cause of death in women ages 45 to 55 years. An estimated 1 million cases of breast cancer are diagnosed annually worldwide. Approximately 5-10% of patients with breast cancer have distant metastases at first presentation. Breast cancer as a biological and genetically heterogeneous tumor often metastasizes to the bone (and other sites) so patients with bone metastases form the largest group of patients with metastatic disease. Approximately 50% of patients with metastatic bone disease have clinical symptoms, and in 4% -7% develop pathological fractures of the long bones. The incidence is significantly high in steroid receptor positive tumors and well-differentiated lesions. Recent data suggest that survival may be improved if disease is controlled by offering loco-regional treatment of the primary tumor in metastatic breast cancer. Chemotherapy or hormone therapy is often the main treatment in these patients without loco-regional treatment (surgery or radiotherapy) except in cases of fungation forms and bleeding. There are studies that have shown that removal of primary tumor at times leads to complete disappearance of metastases and improvement in survival in renal cell carcinoma patients. However, such studies have never been performed in other solid tumors. On the other hand, there is a strong body of evidence in experimental settings showing that removal of primary tumor allows growth of metastasis. There is lack of similar data in humans in clinical settings. This a case report about a 44 years old female patient with breast cancer with diffuse bone metastases at first presentation.

## Case Report

The patient came to the Clinic of oncology and radiotherapy in March 2005 for further treatment with the diagnosis: **Carcinoma metastaticum vertebrae lumbosacralis** diagnosed by CT stereotactic biopsy of L5. The patient has done the following tests: 1. Scan of skeleton: metastatic deposits in spine, rib 7 and 10, manubrium sterni and sacrum; 2. mammography findings were with the presence of malignancy (20,5x13 mm) in left breast with package lymph nodes in the left axilla; 3. FNAB of the breast: was without the presence of malignant cells but from the lymph node of the axilla: deposit of ductal invasive breast cancer. In the context of this patient's clinical stage was: T2N1M1 Gx (Stage. IV). [2] Immunohistochemical findings of metastasis in the vertebra was: HER: negative; ER: 2+/3+; PGR: inconclusive. CEA=9,71 ng/ml; CA15-3: 22,2 U/ml.

**Treatment: Initial treatment 2005:** 6 cycles of chemotherapy (AC protocol - Doxorubicin 60mg/m<sup>2</sup> + Cyclophosphamid 600mg/m<sup>2</sup> intravenous. at 21 days) + bis-

phosphonate therapy (amp. Pamidronic acid a 90 mg, i.v., at 28 days) [5] + realized radiotherapy on L5, TTD = 30Gy, 10fr/3Gy, TCT. Tumor markers at the end of treatment: CEA: 2,38; CA15-3: 19.6. After that a radical mastectomy [6] of the left breast with dissection of left axilla was conducted and pathological analysis showed poorly differentiated ductal invasive carcinoma that infiltrates as ragged sheets of pleomorphic cells with numerous mitotic figures and central areas of tumor necrosis (grade 3 according to Nottingham Histologic Score) with immunohistochemistry findings: HER: negative, ER: negative, PGR: negative or Triple negative breast cancer (TNBC).

The patient was set on hormone therapy: Tabl. Tamoxifen a 10 mg 2x1. In June 2007 patient is started with second-line hormone therapy because for the growth of tumor marker (CEA = 17, 7), progress of metastatic disease and menopause (Aromatase inhibitor - Tabl. Letrozol 1x1). November 2010 due to the progress of bony metastases of the thoracic spine and inability for radiotherapy due to cumulative toxicity of spinal cords from previous radiotherapy to the thoracic spine, bisphosphonate therapy was changed. (Amp. Zolendronic acid a 4mg i.v.)[3,4]

**Results /Follow-up: 2006-2010:** The patient was in good general condition. Continues with intravenous bisphosphonate therapy for 28 days and hormone therapy. Ultrasonography of the breast every 6 months: normal findings. Mammography annually: normal finding. [1] Abdominal ultrasound every 6 months: normal findings. X-rays of the lungs annually: normal findings. Tumor markers analysis every 6 months: in reference. Scan of the skeleton once a year: the appearance of metastases on both shoulders and right sacroiliac articulation, whole thoracic and lumbar spine (2007), left clavicle (2008), the progress of the thoracic spine (2010).

**2011-2013:** Good general condition. Stable metastatic disease. The patient is still on bisphosphonates and hormone therapy. Scan skeleton: Regression of bone metastases. Eight-year survival.

## Discussion

Tremendous international interest has been generated in triple-negative breast cancer, in part because of its poorer overall prognosis and lack of specific targeted therapies. Clinical trials investigating novel treatment strategies in the metastatic setting are essential to improve the survival of this high-risk subgroup.

The results from published literature showed that patients with TNBC have an increased likelihood of distant recurrence and of death compared to women with other types of breast cancer. The pattern of recurrence is also

qualitatively different. Also, according to published literature women with TNBC experience the peak of risk of recurrence within 3 years of diagnosis and increased mortality rates for 5 years from the diagnosis.

In our case report we have an example for 8 year survival that represents the rarest percentile of the general survival rates and also states the individuality in acceptance of the treatment.

### Conclusion

Some of the patients who present with breast cancer already have distant metastatic disease. According to recent literature, these patients may benefit from resection of the breast tumor. One explanation for the effect of this resection is that reducing the tumor load influences metastatic growth. When metastasectomy is not possible, minimally invasive techniques can be used in selected patients for the treatment of breast cancer liver metastases, radiofrequency ablation (RFA) being discussed most in the literature. Results of future randomized controlled trials should indicate whether surgery of the breast tumor truly improves survival and is there any differences between initially bone and parenchymal metastases.

### Acknowledgements

Dr Kristina Todosieva Serafimova & Dr Kristina Nikola Serafimova

### Funding

None.

### Competing Interests

None declared.

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