Spinal Metastases in Breast Cancer: Single Center Experience

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Key words
- Breast cancer
- Spinal metastasis
- Survival
- Treatment
- Tumor board

Abbreviations and Acronyms
CT: Computed tomography
Her2: Human epidermal growth factor receptor 2
HR: Hormonal receptor
MRI: Magnetic resonance imaging
SRE: Skeletal-related events
UICC: Union for International Cancer Control

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Citation: World Neurosurg. (2014) 82, 6:1344-1350. http://dx.doi.org/10.1016/j.wneu.2014.08.010

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

OBJECTIVE: **Metastases to the spine are a common manifestation of breast cancer leading to considerable reduction in the patient's quality of life. Physicians must consider the different treatments available to decrease pain, reduce tumor burden, and ensure spinal stability to prevent neurological compromises. The first objective of this study is to analyze the epidemiology and outcomes of patients with spinal metastases from breast cancer and describe changes over time in these lesions. The second objective is to establish the current treatment of spinal metastases in this type of cancer.**

METHODS: **A total of 140 patients with breast cancer and spinal metastasis involvement were studied retrospectively. Demographic, clinical, and radiologic parameters were assessed, and the effects of systemic and local treatments on spinal metastasis were analyzed.**

RESULTS: **Median patient age at diagnosis of breast cancer was 50 years (19–86 years) and average follow-up was 100 months (4–384 months). Median overall survival after diagnosis of spinal metastasis was 18.6 months. Fractures were present in 24 patients (19.3%) at diagnosis and in up to 60 cases (48.6%) by the end of the study period.**

CONCLUSIONS: **The survival rate was better in patients with spinal metastases who received specific treatment. The evolution from lytic spinal metastasis to mixed and blastic subtypes is observed with adjunctive therapy for spinal metastases (bisphosphonates, radiotherapy). Increased attention must be given for high-grade breast cancer, as spinal metastases declare faster for these stages. This study provides evidence that a multidisciplinary tumor board specifically focusing on bone metastasis is essential to effectively manage patients with breast cancer and spinal metastasis.**

INTRODUCTION

About 20% of patients with breast cancer suffer from bone metastases (4). Skeletal involvement is present in more than half of the cases with distant metastases and spinal metastases are one of the most frequent sites of bony metastasis occurrence in this specific cancer (7, 19, 20, 22). The spinal involvement decreases dramatically the patient's quality of life. Thus it is important to investigate different strategies to decrease pain, reduce tumor, and to correct sagittal spinal balance to prevent spinal cord injury. A multidisciplinary tumor board allows the coordination of all specialists to optimize treatment of spinal metastasis from breast cancer.

Different clinical and skeletal-related events (SRE) such as pain, pathologic fracture, neurologic compression, hypercalcemia, and medullary insufficiency occur as a consequence of spinal metastasis evolution.

At present there is no consensus guiding the follow-up of bone metastasis treatment from diagnosis through various available strategies. Recent (<3 months) computed tomography (CT) scan and magnetic resonance imaging (MRI) are essential to evaluate skeletal integrity and/or the effect on spinal cord and nerve roots. Spinal metastasis can be diagnosed by an initial single photon emission CT. In case of positivity, a CT and/or MRI are performed to evaluate the location and severity of the lesion(s) (21).

Ongoing treatments of spinal metastasis from breast cancer include chemotherapy, hormonotherapy, bisphosphonates, radiotherapy, vertebroplasty, surgery (to ensure spinal stability, correct deformity, and decompress neural elements), and metabolic radiotherapy with samarium (15, 24). These interventions reduce tumor burden and pain, and can induce a spinal stabilization and a neural protection.

The aim of the present study was to retrospectively analyze the epidemiology and outcomes of patients with spinal metastases from breast cancer and describe changes over time in these

lesions. The secondary objective was to show the interest of a mutlidisciplinary team tumor board. We compared the clinical and biologic evolution of breast cancer spinal metastasis treated with current methods guided by tumor board to previously published studies.

METHODS

Patient's Data

This retrospective cohort study included all patients diagnosed for breast cancer who were discussed in a multidisciplinary tumor board during the period 2009–2012 at one Regional Institute of Cancer (Institute of Cancer from Montpellier, France). This study was restricted to patients with spinal metastases from breast cancer to limit differences as a result of variation in primary cancer subtypes. For these patients, we retrospectively reviewed all the data from the initial diagnosis of breast cancer.

For each patient, age at diagnosis of breast cancer, histologic subtype of breast cancer, stage (according to the Union for International Cancer Control [UICC] system), treatments, clinical/biologic evolution of cancer, spinal metastasis events, Tokuhashi and Tomita scoring system for preoperative evaluation of metastatic spine tumor prognosis, and date of death were recorded by electronic chart review. Radiologic characteristics of spinal involvement, such as lytic/osteoblastic/mixed lesion, presence of metastatic arachnoiditis, paravertebral extension, fractures, and/or kyphosis, were discussed after primary review of spine CT and/or MRI.

Radiologic Characteristics Analysis

Review of CT and MRI determined the topography of lesions (cervical, thoracic, lumbar), Tokuhashi and Tomita score, lytic, osteoblastic or mixed characteristics of spinal metastasis, presence of metastatic arachnoiditis and/or paravertebral extension, fractures, and/or spinal static imbalance. The same analyses were performed during the follow-up. The distribution rate of lytic, osteoblastic, and mixed spinal metastases was calculated just after the diagnosis and during follow-up.

Statistical Analysis

Data were analyzed using one-way analysis of variance when we compared more than 2 groups (e.g., to compare different characteristics according to the stage of breast cancer) and Fisher's test to underline a difference between 2 groups within a category (e.g., to assess the effect of treatments on bone condensation). A P value < 0.05 was considered statistically significant (Graphpad Prism, version 6, La Jolla, California, USA).

RESULTS

Between 2009 and 2012, 140 patients with breast cancer and spinal metastasis involvement were treated. The average follow-up of our population was 100 months (range, 4–384 months). Median age at diagnosis of breast cancer was 50 years (range, 19–86 years). Anatomic and pathologic characteristics of our breast cancer population are shown in Table 1. Forty-eight deaths occurred during the follow-up period (34% of the population), with a median age at death of 59.5 years(range, 22–87 years).

Diagnosis of spinal metastasis from breast cancer in asymptomatic patients was done during systematic routine follow-up in 35% of cases (bone scintigraphy [single photon emission CT-CT], whole-body CT scan, or MRI). Axial and/or radicular pain prompted us to identify spinal metastasis for 63.3% of patients. In 2 cases (1.4%), an overt neurological deficit led to the diagnosis of spinal metastasis. During the follow-up period, 4 patients (2.8%) developed clinical symptoms of spinal cord compression.

SREs were observed in 49 patients and included pain (73%), pathologic fracture (18%), and neurological deficit (9%). The average survival time without a SRE was 58.7 months (median, 28 months) after the spinal metastasis diagnosis. At the end of the study, 73 patients (52%) had no SRE. For patients with a second independent SRE, the median delay between 2 SREs was 13 months.

The delay between breast cancer diagnosis and spinal metastasis diagnosis events significantly differed according to UICC stage criteria (overall $P< 0.05$, Fisher's test). Spinal metastasis occurred after a median delay of 88.5 months for stage I, 74 months for stage II, 24 months for stage III, and 0 months for stage IV (Figure 1). This trend toward a shorter period to diagnosis of spinal metastasis with worsening clinical status was similar if we partitioned by TNM classification.

We analyzed our cohort according to the hormonal receptor (HR) and/or human epidermal growth factor receptor 2 (Her2) protein status (Table 2). We showed a longer delay of spinal metastasis diagnosis for the HR−/Her2− group (median, 45.5 months) compared with HR+/Her2− (median, 28 months) and HR+/Her2+ (median, 3 months) groups

Table 1. Histologic Characteristics and Breast Cancer Classification

	Number of Patients	Percentage (%)
Histologic characteristic		
Ductal carcinoma	89	62.2
Lobular carcinoma	26	18.2
Mixed	4	2.8
Sarcoma	3	2.1
Unknown	21	14.7
Hormonodependance		
+	95	68
–	20	14
Unknown	25	18
Her2 protein		
+	21	14.7
–	79	55.2
Unknown	43	30.1
TNM		
T0	2	1.4
T1	30	21.4
T2	36	25.7
T3	15	10.7
T4	17	12.2
Stage according to UICC		
I	16	11.4
II	32	22.9
III	19	13.6
IV	48	34.3
Unknown	25	17.9

Her2, human epidermal growth factor receptor 2; UICC, Union for International Cancer Control.