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Skeletal metastases in non-small cell lung cancer: A retrospective study

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Summary
Background: The skeleton is one of the most common sites of metastasis in patients with advanced cancer. Bone metastases often cause SREs (skeletal-related events). Despite advances in the treatment of primary lung cancer, SREs still affect many patients. Therefore, we planned a retrospective study to investigate the clinical impact of SREs, and to compare differences in the therapeutic outcome between patients with and without skeletal metastases or SRE.
Patients and methods: We retrospectively investigated the charts of all 259 patients with non-small cell lung cancer (NSCLC) who consulted the Department of Medical Oncology at Kinki University School of Medicine between February 2002 and January 2005. We assessed their TNM stage, presence of skeletal metastases (on bone scintigraphy, MRI, and plain X-ray films), and outcome parameters such as SREs, analgesic use, and survival.
Results: A total of 70 patients (30.4%) were found to have skeletal metastases during their clinical course and 35 patients (50%) out of all 70 patients had SREs. Among 135 stage IV patients, a total of 56 (41%) had skeletal metastases, and 25 of these 56 patients (45%) had SREs. The most common SREs were the need for radiotherapy (34.3%) and hypercalcemia (20%). Patients with SREs tended to have worse survival, while no significant difference of survival was observed between patients with and without skeletal metastases.
Conclusion: It seems to be important to prevent SREs during the treatment of NSCLC, so further studies evaluating bisphosphonates in combination with chemotherapy are warranted.

1. Introduction

Most patients with advanced cancer develop skeletal metastases during the course of their disease, and these are often associated with significant morbidity [1]. The major-

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ity of bone metastases arise from primary tumors of the breast, prostate, thyroid, or lung among others. In Western countries, it has been reported that the incidence of bone metastases in lung cancer patients is approximately 30—40%, and the median survival time (MST) of patients with such metastases is 7 months [2]. A more recent retrospective review of 435 patients with non-small cell lung cancer (NSCLC) revealed an incidence of 24% for skeletal metastases. In this review, the majority of skeletal metastases (66%) were detected at the time of initial staging [3]. Bone is a common site of cancer spread, ranking only behind the liver and the lungs in frequency.

Despite advances in the treatment of primary lung cancer, skeletal-related events (SREs) still affect many patients during their clinical course. Common complications of skeletal metastasis include bone pain, symptomatic pathologic fracture, spinal cord compression, and hypercalcemia of malignancy (HCM). These complications often require surgery to correct fractures or spinal deformities and/or radiation therapy to control the severe pain that is a hallmark of bone metastases. Pain due to bone metastases is the most frequent form of pain reported by cancer patients [4]. Thus, SREs have a negative impact on the quality of life, performance status, and function of cancer patients.

Although skeletal metastases due to lung cancer have already attracted attention in Western countries, little is known about the incidence of bone metastases arising from lung cancer in Japan. Therefore, we planned a retrospective study to investigate the clinical impact of SREs and to explore the therapeutic outcome of patients with or without skeletal metastases and/or SREs.

2. Patients and methods

2.1. Study population

We retrospectively investigated 259 patients with NSCLC who consulted the Department of Medical Oncology at Kinki University School of Medicine between February 2002 and January 2005.

The TNM stage, the presence of skeletal metastases (on bone scintigraphy, MRI, and plain X-ray films), and outcome parameters such as SREs, analgesic use, and survival were investigated.

In this study, SREs were defined as pathologic fracture, spinal cord compression, hypercalcemia, bone radiation therapy (palliative therapy for pain, or treatment/prevention of pathologic fractures and spinal cord compression), and bone surgery (stabilization or decompression).

2.2. Statistical analysis

The characteristics of stages III and IV patients were compared using the χ^2-test. Survival curves were calculated and drawn by using the Kaplan—Meier method, and differences between stage IV patients with or without SREs were assessed by the log—rank test. All analyses were two-sided. Statistical software (Statistical Package SAS Software release 8.2) was used for statistical analysis, and $p < 0.05$ was considered statistically significant.

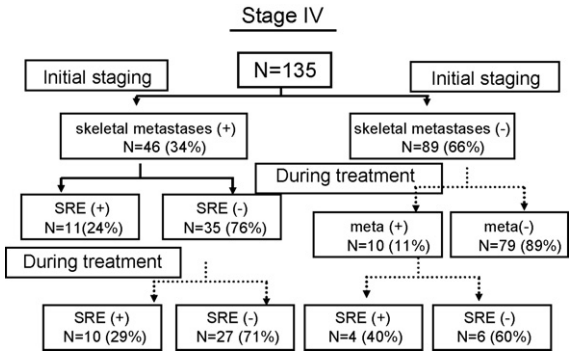

Fig. 1 Incidence of skeletal metastases and SREs in patients presenting with stage IV disease.

3. Results

3.1. Patients

We retrospectively investigated 259 NSCLC patients who visited and consulted the department of Medical Oncology, Kinki University School of Medicine, between February 2002 and January 2005. A total of 29 patients were excluded because of early stage disease, so the total number of patients assessed was 230. Among them, 156 patients (68%) were men. The pathologic diagnosis was adenocarcinoma in 140 patients (61%) and most patients had a good performance states (PS 0/1 in 193 patients, or 84%). The median age was 65 years. There were no obvious difference of these characteristics between patients in stage III and stage IV, although statistical analysis was not done.

3.2. Incidence of skeletal metastases

A total of 70 patients (30.4%) were found to have skeletal metastases during their clinical course. Among them, 46 patients (65.7%) had skeletal metastases at the time of initial diagnosis. Thirty-five (50%) of the 70 patients suffered from SREs. Eleven (31%) of the 35 patients had SREs at the time of initial staging, and 24 (69%) of the 35 patients developed SREs due to recurrence of their disease after treatment.

Of the 135 patients who were initially in stage IV, 56 patients (41%) had skeletal metastases, and 25 (45%) of these 56 patients suffered from SREs. Among the 56 patients with skeletal metastases, 46 patients (82%) had these metastases at the time of initial staging, while 11 (44%) of the 25 patients with SREs already had them at initial staging (Fig. 1).

A total of 95 patients were initially in stage III. After treatment of their cancer, 14 patients developed skeletal metastases and 10 (71%) of them suffered from SREs (Fig. 2).

3.3. Sites of skeletal metastasis

Table 1 shows the sites of skeletal metastasis. The spine was the most common site (50%), followed by the ribs (27.1%).