



Research Paper

Prognostic and risk factors in patients with metastatic bone disease of an upper extremity

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ABSTRACT

Background: The aim of this study was to evaluate survival of metastatic bone disease of an upper extremity, and to identify the prognostic factors that influence survival.

Methods: Patients with metastatic bone disease of an upper extremity between 2008 and 2015 were reviewed from the database of a tertiary university hospital.

Results: Of 102 patients, 48 males and 54 females with a median age of 61 (range, 28–82 years), the humerus (64.7%), clavicle (13.7%), and scapula (12.7%) were the common sites for bone metastasis of an upper extremity. Fifty-nine (57.8%) presented with pathologic fracture. No history of cancer was found in 76.5% of patients. The mean onset of metastatic bone disease after the first diagnosis of primary cancer was 4.74 ± 14.07 months (range, 0–84 months). Lung (31.4%) was the most common primary cancer followed by liver (14.7%), breast (12.7%), thyroid (7.8%), and renal (3.9%). Eighty-two cases (80.39%) died from the disease such that the median survival was 4.08 months (95% CI 2.57–6.17). The significant risk factors were the type of primary tumor ($P < 0.001$, HR = 4.44; 95% CI, 1.99–9.90) and ECOG performance status ($P = 0.021$, HR = 2.11, 95% CI 1.12–3.99).

Conclusions: Patients with metastatic bone disease of an upper extremity have a limited life expectancy. The type of primary tumor and ECOG performance status were the important prognostic factors that influenced overall survival. Our data help in the management of patients, families, and doctors, so as to avoid over- or under-treatment.

1. Introduction

As treatment of cancer improves, patients have an increasing life-expectancy but also an increased risk of metastatic bone disease. Patients with metastatic bone disease can present with or without a history of cancer. When they present with bone symptoms—i.e., pain or pathological fracture—the existence of a primary tumor must be ruled out. Examples of typical primary tumors frequently associated with metastasis to bones are lung, breast, kidney and prostate [1].

The treatment of metastatic bone disease includes surgery, chemotherapy, and radiation. The choice of surgical procedures in metastatic cancer depends upon the estimated survival of the patient. In patients with a relatively long predicted survival, aggressive treatment (s) and durable implants are appropriate. In cases where life expectancy is short, less invasive or palliative treatment are indicated [2]. Previous studies have indicated that the prognostic factors for metastatic bone

disease include age, primary tumors, onset of bone symptoms, pathological fracture, metastasis to other organs, performance score, and pre-operative hemoglobin level [1,3–9]. Previous studies regarding the prognostic factors and survival of metastatic bone disease were, however, not specific to metastatic bone disease of an upper extremity [6].

To the best of our knowledge, this is the first study to describe prognostic and risk factors in patients with the metastatic bone disease of an upper extremity—with the primary tumor being a solid organ. The present study, set at a tertiary university hospital, was conducted (a) to evaluate survival of metastatic bone disease of an upper extremity, and (b) to identify the prognostic factors that influence survival.

2. Methods

The ethics committee at our institution reviewed and approved the protocol. The authors reviewed all records of patients diagnosed with

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metastatic bone disease of an upper extremity between 2008 and 2015 at the Musculoskeletal Oncology Unit, at our tertiary university hospital. The inclusion criteria were patients who presented initially with metastatic bone lesions only in an upper extremity. The exclusion criteria were primary bone tumors. The latter being a hematologic malignancy (i.e., multiple myeloma or lymphoma).

The data reviewed were from the Cancer Registry, Srinagarind Hospital, Khon Kaen University, Thailand. The data from 102 patients with metastatic disease of an upper extremity alone were obtained. The retrieved data were age at diagnosis of bone metastasis, history of cancer, type primary tumor, onset of metastatic bone disease after the first diagnosis of primary tumor, presenting with or without pathologic fracture, performance score, location of bone lesion, and visceral and skeletal metastases. Investigations included plain X-ray of the affected limb, chest X-ray, and computed tomography (CT) scan of chest, abdomen, pelvis, and bone. All investigations were performed before a biopsy was done. All pathology slides were reviewed by a single musculoskeletal oncology pathologist.

3. Statistical analysis

Overall survival time was calculated from the time of admission to our hospital to death or last follow-up visit. The survival analysis was calculated using life table analysis and Kaplan–Meier method. The following parameters: age, sex, onset of metastatic bone disease, primary tumors, Site of metastasis, visceral metastasis, pathological fracture, and performance score were analyzed for validity as prognostic factors. Each prognostic factor was categorized for statistical analysis. Age group was categorized into <60 or ≥60 years. Onset of metastatic bone disease was categorized into no known history of tumor, 1–12 months and >12 months after diagnosis of primary tumor. Primary tumors were categorized according to median survival time into slow (>20 months), moderate (10–20 months) and rapid growth (<10 months) [10]. Visceral metastasis was divided into two groups: with or without metastasis. Pathological fracture was divided into two groups: present or absent fracture. Eastern Cooperative Oncology Group Performance Status (ECOG PS) was used to evaluate the performance status of the patients, and was categorized into two groups: ECOG PS 0–2 and 3–4 [10]. Site of metastasis was divided into proximal and distal to the elbow joint.

The log–rank test was used to screen for potential prognostic value; if any test was significant ($P < 0.2$) then a Cox regression analyses was performed. P values < 0.05 were considered to be statistically significant.

All statistical analyses were conducted using SPSS 19.0 statistical software (SPSS, Chicago, IL, USA).

4. Results

4.1. Patient characteristics

The demographic data are presented in Table 1. Of the 102 patients, 48 were males (47.1%) and 54 were females (52.9%). The median age was 61 years (range, 28–82 years). Fifty-nine (57.8%) patients presented with pathologic fracture. No history of cancer was found in 78 (76.5%) cases. The mean onset of metastatic bone disease after the first diagnosis of primary cancer was 4.74 ± 14.07 months (range, 0–84 months). The rank of site of bone metastasis was the humerus (64.7%), clavicle (13.7%), and scapula (12.7%). Acral metastasis (lesion below the elbow) occurred in 7.8% (Table 1).

The most common primary tumor was lung (31.4%) followed by liver (14.7%), breast (12.7%), thyroid (7.8%), kidney (3.9%), bile duct (cholangiocarcinoma) (2.9%), nasopharynx (2%), and 1% each for the colon, cervix, bladder, endometrium, and esophagus. Adenocarcinoma of unknown origin was 19.6% (Table 2). In 8 cases of acral metastasis, the primary tumor was lung in 7 cases and adenocarcinoma of unknown

Table 1
Demographic data.

Characteristic	Patients (N = 102)	(%)
Sex		
Male	48	47.1
Female	54	52.9
Age		
<60 years	50	49
≥60 years	52	51
History of cancer		
Present	24	23.5
Not present	78	76.5
Onset of bone metastasis after diagnosis of primary tumor		
0 month	78	76.5
1–12 months	14	13.7
>12 months	10	9.8
Pathologic fracture		
Present	59	57.8
Absent	43	42.2
Tumor location		
Scapula	13	12.7
Clavicle	14	13.7
Humerus	67	65.7
Radius	3	2.9
Ulna	2	2
Hand	3	2.9
Visceral metastases		
Present	62	60.8
Not present	36	35.3
Unknown	4	3.9
ECOG performance status		
1	28	27.5
2	49	48
3	23	22.5
Unknown	2	2

Table 2
Primary tumors and median survival time.

Primary tumors	N	Median survival (months) (95% CI)
Slow growth		
Endometrium	1	127.13
Moderate growth		
Breast	13	11.67 (1.98–32.58)
Thyroid	8	11.63 (4.3–14.0)
Nasopharynx	2	10.12
Rapid growth		
Lung	32	5.4 (2.27–8.8)
Adenocarcinoma of unknown origin	20	1.97 (1.32–7.90)
Liver	15	2.5 (0.92–4.08)
Renal	4	4.31
Bile duct (cholangiocarcinoma)	3	2.1 (0.13–4.07)
Colon	1	0.33
Cervix	1	6.53
Bladder	1	4.53
Esophagus	1	2.23

origin in 1 case.

The treatments were surgery in 50% of cases, palliative treatment in 44.2% and radiation alone in 5.8%. The surgical procedures included excision (7.8%), cementing after tumor curettage and internal fixation with intramedullary nailing (32.4%), plate and screw (7.8%), endoprosthesis (2%).

4.2. Outcome

No patient was lost to follow-up. Eighty-two (80.4%) patients died from the disease with a median survival of 4.08 months (95% CI 2.57–6.17) (Fig. 1). Further analysis was done of 101 of the total 102 cases who had a survival time <64 months. The median survival time was 4.53 months (95% CI 1.84–7.22). None of the patients died from

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