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Bone metastases

The incidence of neuropathic pain in bone metastases patients referred for palliative radiotherapy

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ABSTRACT

Background and purpose: To estimate the prevalence of neuropathic pain in patients with symptomatic bone metastases referred for palliative radiotherapy.

Material and methods: A prospective study of patients with symptomatic bone metastases was conducted. Patients referred for palliative radiotherapy completed the Self-Reported Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire to assess for neuropathic pain. Patient demographics, medication use, and radiotherapy prescribed were collected. Statistical approaches to identify relationships between the presence of neuropathic and other patient factors were conducted.

Results: 62 patients completed the S-LANSS and 16 (25.8%) patients had a score suggesting neuropathic pain. Fifty-nine (95.2%) patients received radiotherapy with total of 81 sites treated, the most common sites were spine and pelvis. No statistically significant difference in fractionation was found between patients with and without neuropathic pain. Of the 16 patients with neuropathic pain, only 2 were receiving a neuropathic specific analgesic. No significant difference between demographic factors or radiation treatments between patients with and without neuropathic pain was found. There was no significant difference in worst pain score between these two groups.

Conclusions: Pain with neuropathic features remains prevalent in a population of patients referred for palliative radiotherapy. More frequent prescription of pain medications targeting neuropathic pain may be warranted in this patient population.

Bone is a common site of metastases from various primary cancers including prostate, breast, and lung cancer [1]. Skeletal metastases are often symptomatic, with pain being the most frequent symptom experienced by 60–70% of patients [2]. Bone metastases can be associated with neuropathic pain, characterized as pain in an area with tissue damage and attributable to compression or injury of a neural structure [3].

Neuropathic pain from bone metastases can result from pressure on neural structures, due to malignant extension as well as from plasticity of the nervous system [3]. Typical characteristics of neuropathic pain can include burning, stabbing, shooting or electric shock-like sensations [3]. Neuropathic pain is often associated with sensory, motor, or autonomic dysfunction [3]. Unfortunately, for many patients neuropathic pain is often associated with suffering, disability, and reduced health-related quality of life [4]

An effective treatment option for symptomatic bone metastases is palliative radiotherapy. Radiotherapy in single fraction and multiple fraction regimens is efficacious in palliating painful uncomplicated bone metastases [5,6]. Studies have also shown that there is a role for radiotherapy in the treatment of symptomatic bone metastases with neuropathic pain features [7,8].

Neuropathic pain has certain characteristics that distinguish it from simple uncomplicated bone pain. It is important to use these features to identify pain as neuropathic in nature in order to confirm the site of origin and prescribe effective methods of treatment [9]. The objective of our present study was to examine the prevalence of pain with neuropathic features in patients referred for palliative radiotherapy to symptomatic bone metastases.

Methods

In order to examine the incidence of neuropathic pain in patients referred to a specialized rapid access palliative radiotherapy clinic, a prospective cross-sectional study of patients with symptomatic bone metastases was conducted from November

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2014 to June 2015. Ethics approval was obtained from the Sunnybrook Research Ethics Board.

Patient population

All patients referred to the Rapid Response Radiotherapy Program (RRRP) at the Sunnybrook Odette Cancer Centre for symptomatic bone metastases from all primary cancer sites were eligible for inclusion in the study. Patients in this study did not have neurological or clinical signs of spinal cord compression. The patients included had uncomplicated bone metastases or with neuropathic pain features. All eligible patients were approached to complete the questionnaire.

Neuropathic pain evaluation

Patients were asked to complete the Self-Reported Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire with a clinical research assistant in the clinic during their visit. This 7 item questionnaire assesses items including appearance of painful area, sensitivity to touch, burning or needle-like pain, and other identifying characteristics of neuropathic pain [10]. The questionnaire was scored with a maximum score of 24 when all items are affirmative, and a score greater than or equal to 12 indicates that there is a neuropathic component to the subject's pain [10].

Statistical analysis

Patient demographics, information regarding to analgesic use and pain characteristics, and all responses to the questionnaires were collected from the Sunnybrook Electronic Patient Record. Descriptive statistics were summarized using mean, standard deviation (SD), interquartiles, median and ranges for continuous variables, and proportions for categorical variables. To compare demographics and clinical factors between patients with or without neuropathic pain, Wilcoxon rank-sum nonparametric test, Fisher exact test, or Pearson Chi-square test was applied for continuous variables (i.e., worst pain score and effective dose), dichotomous variables (i.e., age > 65, KPS > 70, gender, single or multiple fractions), or categorical primary cancer site variable. To account for these multiple comparisons, Bonferroni adjusted p-value < 0.007 was considered statistically significant. All statistical analyses were performed using the Statistical Analysis Software (SAS version 9.4 for Windows).

Results

Patient demographics

A total of 62 patients completed the S-LANSS and 19 declined to participate (response rate of 76.5%). Patient demographics are detailed in Table 1. There were 28 female (45.2%) and 34 male (54.8%) patients included with a median age of 67 years. The majority of participants were outpatients (85.5%) and the median KPS was 70. Prostate (37.1%), lung (19.4%), breast (17.7%) and gastrointestinal (14.5%) cancer were the most frequently reported diagnoses (Table 1).

Patient analgesic use

Fifty-seven patients (91.9%) were using analgesic for pain control at the time of consultation, and five (8.1%) were not. Full description of pain medications is given in Table 2. Among the 57 Patients receiving pain medication, the most common analgesics used were hydromorphone and acetaminophen. Only three (5.3%) and 4 (7.0%) patients were using gabapentin and pregabalin, respectively.

Table 1
Demographics of study participants (n = 62).

Patient factor	Value	
Age (years)		
Median (Range)	67 (46–92)	
KPS		
Median (Range)	70 (30–90)	
	N	(%)
KPS ⩽ 70	37	(59.7%)
KPS > 70	25	(40.3%)
Gender		
Male	34	(54.8%)
Female	28	(45.2%)
Patient status		
Inpatient	9	(14.5%)
Outpatient	53	(85.5%)
Primary cancer site		
Prostate	23	(37.1%)
Lung	12	(19.4%)
Breast	11	(17.7%)
GI	9	(14.5%)
Others	7	(11.3%)

Table 2
Summary of participant analgesics at time of assessment.

Description	*n*	(%)
Current pain medication (n = 62)		
No	5	(8.1%)
Yes	57	(91.9%)
Description of pain medications (n = 57 patients)		
Opiod and Acetaminophen		
Acetaminophen	20	(35.1%)
Hydromorphone	25	(43.8%)
Oxycodone	6	(10.5%)
Oxycodone + Acetaminophen	4	(7.0%)
Fentanyl	2	(3.5%)
Morphine	2	(3.5%)
Non-steroidal anti-inflammatory (NSAID)		
Ibuprofen	1	(1.8%)
Celecoxib	1	(1.8%)
Naproxen	1	(1.8%)
Ketorolac tromethamine	1	(1.8%)
Anticonvulsant and Analgesic		
Gabapentin	3	(5.3%)
Pregabalin	4	(7.0%)

Neuropathic pain features

Of the 62 patients that completed the S-LANSS questionnaire, 16 (25.8%) patients had a total score greater than or equal to 12, suggesting neuropathic pain. The median worst pain score was 7 out of 10. The detailed summary of the questionnaire results is outlined in Table 3. Further data in the Supplementary material also summarize responses to each of the 7 questions in patients with or without neuropathic pain.

Radiation treatment

Out of 62 patients that completed the study, 59 (95.2%) patients received radiation treatment and a total of 81 sites were treated. Of the remaining 3 patients (4.8%) that did not receive radiotherapy, 1 declined treatment, 1 was referred for neurosurgery, and 1 was referred to a multidisciplinary bone metastases clinic for consideration of orthopedic intervention. A single fraction of 8 Gy was pre-