Original Article

Strategy for Bone Metastases Treatment in Patients with Impending Cord Compression or Vertebral Fractures: A Pilot Study

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Abstract

Impending spinal cord compression and vertebral fractures are considered contraindications for radionuclide bone pain palliation therapy. However, most of the patients with widespread bone metastases already have weakened vertebral segments that may be broken. Therefore, local field external-beam radiotherapy or percutaneous vertebroplasty (VP) should be considered to improve the patient’s quality of life and to institute subsequent appropriate treatment, including radionuclide therapy for bone pain palliation. The objective of this study was to develop a strategy for an effective treatment of bone metastases in patients with widespread bone metastases and intolerable pain, associated with impending cord compression or vertebral fractures. Eleven patients (5 females and 6 males, aged 32–62 years; mean age 53.8 ± 2.7 years) with multiple skeletal metastases from carcinomas of prostate (n = 3), breast (n = 3) and lung (n = 5) were studied. Their mean pain score measured on a visual analogue scale of 10 was found to be 8.64 ± 0.15 (range 8–9) and the mean number of levels with impending cord compression or vertebral fracture was 2.64 ± 0.34 (range 1–4). All patients underwent vertebroplasty and after 3–7 days received Sm-153 ethylene diamine tetra methylene phosphonic acid (EDTMP) therapy. Sm-153 EDTMP was administered according to the recommended standard bone palliation dose of 37 MBq/kg body weight. Whole body (WB) bone scan, computed tomography and magnetic resonance imaging (MRI) were performed before and after treatment in all patients. Pain relief due to stabilization of vertebrae after VP occurred within the first 12 hours (mean 4.8 ± 1.2 hours; range 0.5–12 hours), and the mean pain score was reduced to 4.36 ± 0.39 (range 2–6). Subsequent to Sm-153 EDTMP treatment, further pain relief occurred after 3.91 ± 0.39 days (range 2–6 days) and the pain score decreased to 0.55 ± 0.21 (range 0–2). The responses to treatment were found to be statistically significant (P < 0.0001). Based on the results on this limited patient population, we conclude that spinal stabilization using VP in patients with widespread bone metastases and impending cord compression is an effective way to decrease disability with pain and to facilitate subsequent systemic palliation of painful skeletal metastases by Sm-153 EDTMP therapy.

Keywords: Bone pain palliation, Sm-153 EDTMP, vertebroplasty

Introduction

Bone metastasis remains a major cause of morbidity in patients with cancer and represents a common manifestation of the disease. It occurs in 65–75% of patients with cancers of the breast and prostate, 30–40% of patients with lung cancer, a and significant proportion of patients with cancers of the thyroid, bladder and kidney.[1] In patients with non-small cell lung cancer, 70% of patients with bone metastases have bone pain.[2-3] According to Varadhachary, 60–84% of all cases of metastatic disease invade bone and approximately 70% of patients with metastatic bone disease experience bone pain.[4]

The vertebral column is the most common site for bone metastases, with an incidence of 30–70% in patients with
metastatic neoplasms.\textsuperscript{[5-7]} Patients with metastatic cancer involving bone are also at increased risk of fractures, spinal cord compression (SCC), hypercalcemia, and immobility, resulting in substantial medical-associated morbidities. Jensen \textit{et al.} reported high incidence of skeletal-related events (SREs) in Denmark’s population among women with breast cancer. According to this data, SREs were the highest during the first year after the primary diagnosis of bone metastases and occurred in 47.6\% of breast cancer’s patients.\textsuperscript{[8]}

Mechanical pain usually is associated with bone loss in lytic lesions; however, blastic lesions may weaken the bone sufficiently through the loss of structural integrity to cause functional pain. Progressive involvement of the bone cortex weakens the axial strength of the bone and gives rise to instability.\textsuperscript{[9]} At this stage, more than 50\% of patients with multiple skeletal metastases have ineffective chemotherapy.

Radiotherapy is often highly effective for individual bone metastatic lesions, but its use may be limited in patients with widely metastatic bone disease and disparate areas of pain.\textsuperscript{[10]} Furthermore, even when one site of pain is being treated, other areas outside the radiation field may become symptomatic.\textsuperscript{[11]} Moreover, external beam radiation remains the standard of care for patients with localized bone pain but no impending risk of fracture.\textsuperscript{[12]} While it is effective at reducing tumor volume, it is not helpful to prevent pathologic fracture because it does not strengthen the anterior support of vertebral body.\textsuperscript{[13]}

Role of vertebral metastases in worsening the quality of life is more and more emphasized, but the treatment is still controversial.\textsuperscript{[14]}

Advantages of bone palliation by radionuclide therapy include the ability to simultaneously treat multiple sites of disease.\textsuperscript{[15]} Unfortunately, impending cord compression and vertebral fractures are considered as contraindications for radionuclide bone therapy. However, most of the patients with widespread bone metastases already have weakened vertebral segments that may be broken. Therefore, stabilizing procedure, such as percutaneous vertebroplasty (VP), should be proceeded to enable radionuclide bone therapy.

VP is a minimal invasive technique consisting of percutaneous injection of polymethyl methacrylate (PMMA) into vertebral body to strengthen it and reduce the pain.\textsuperscript{[16]}

Many authors consistently reported the advantage of percutaneous VP for the treatment of tumorous spinal lesion. However, there is no report presenting the clinical outcome of percutaneous VP as a procedure preceding radionuclide bone therapy. In addition, we could get a good clinical result from this type of treatment. Therefore, we report here the clinical results of these consecutive treatments.

**Patients and Methods**

**Patients**

During the period December 2007 to December 2010, we treated 11 patients (5 females and 6 males, aged 32–62 years, mean age 53.8 ± 2.7 years) with multiple skeletal metastases from prostatic carcinoma (\(n = 3\)), breast carcinoma (\(n = 3\)) or lung carcinoma (\(n = 5\)). All patients were referred by Tashkent’s Oncology Centers and by South Kazakhstan Oncology Clinic (Chimkent, Kazakhstan). Pain assessment was based on a visual analogue scale (VAS); on this scale, 0 means no pain and 10 means intolerable pain. Their mean objective pain score before treatment was 8.64 ± 0.15 (range 8–9). Types and doses of the prescribed analgesics were recorded, and pain assessment was repeated after VP and after Sm-153 EDTMP treatment.

Computed tomography (CT) and magnetic resonance imaging (MRI) examinations confirmed the number and levels of vertebral bodies with impending cord compression or vertebral fracture as well as the anatomical features. Mean number of levels with impending cord compression or vertebral fracture was 2.64 ± 0.34 (range 1–4) [Figure 1].

**Vertebroplasty**

VP by percutaneous transpedicular injection of bone cement into the vertebral body was performed on Philips Allura Xper FD 20 by an orthopedic surgeon and an interventional radiologist. VP was performed in

![Figure 1: Patient with NSCLC with widespread bone metastases: multiple osteolytic and osteoblastic lesions and fracture in T-5, T6, and T-10 vertebrare](image-url)
all patients in prone position under local anesthesia. An
anesthesiologist monitored the patient throughout the
procedure. Skin entry points were made about 1 cm from
the lateral edge of vertebrae under C-arm fluoroscopic
guidance [Figure 2].

A VP needle was inserted through pinpoint skin incision.
First, VP needles were inserted until the tips reached the
pedicle base on the C-arm lateral view. Then, the VP
needle tips were checked and after confirmation that
the VP needle did not invade neural canal, VP needle
tips were advanced into the anterior one-third of the
vertebral body on C-arm lateral view. VP needle tips
crossed the midline of vertebral body on C-arm AP view
at the same time. Bone cement was injected to vertebral
body VP needles with C-arm lateral guidance, until it was

Figure 2: Percutaneous trans-pedicular injection of bone cement into the vertebral body
well distributed on both AP and lateral C-arm views. VP may be performed by unilateral or bilateral approach, depending on the surgeon’s preference.

Sm-153 EDTMP therapy
Inclusion criteria for therapy were intense uptake around painful metastases on recent (2–4 weeks before treatment) Tc99m methylene diphosphonate (MDP) whole body (WB) bone scan, hemoglobin >90 g/L, white blood cell count >4 × 10^9/L and platelet count of >100 × 10^9/L. Prior to the administration of the radiopharmaceutical, the patients received information both orally and in a written pamphlet about the procedure, including an explanation of the therapeutic procedure; estimation as to when pain relief may be expected; a warning that a transient flare effect of pain may occur, and therefore, analgesic medication must be continued; radiation protection guidelines, for example, regarding contact with partner, and for pregnant women, children; hygienic measures (e.g. micturition while seated, how to deal with contamination). Also, they were advised that in case of hospitalization or other medical care within 30 days, the physician must be informed, as the therapy may influence other scintigraphic procedures and the patients should carry a medical declaration and radiation safety certificate when traveling shortly after therapy because of airport security checks.

All patients received Sm-153 EDTMP therapy 3–7 days after VP. Sm-153 EDTMP was administered at the standard bone palliation dose of 37 MBq/kg body weight of patient. Tc99m MDP WB bone scan, CT and MRI were repeated 3–8 months after treatment.

Statistical analysis
The acquired results were expressed as the mean ± SEM for each index. Comparison of data amongst various groups was performed with student’s unpaired t-test for normal distributed values. P value of <0.05 was considered statistically significant.

Results
According to our data, pain relief due to stabilization of vertebrae after VP occurred within a relatively short time – during the first 12 hours (mean 4.8 ± 1.2; range 0.5–12 hours), and the mean objective pain score was reduced to 4.36 ± 0.39 (range 2–6) [Figures 3 and 4].

However, patients still had pain due to bone metastases. After subsequent Sm-153 EDTMP treatment, further pain relief occurred after 3.91 ± 0.39 days (range 2–6 days) and the objective pain score decreased further to 0.55 ± 0.21 (range 0–2). There was statistically significant difference between objective pain score before and after treatment.
However, prophylactic VP has been performed to both primary and metastatic spinal tumor as one of the most useful treatment options and it has provided apparent improvement of axial mechanical pain for those patients via strengthening of vertebral body support.\(^{21}\)

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The gold standard treatment of solitary metastatic spinal lesion is en bloc vertebrectomy; however, not all patients with spine metastases can be candidates for this extensive surgery and most patients present to the spinal surgeon with multiple metastases already at the time of diagnosis.\(^{20}\)

Percutaneous VP has been performed to both primary and metastatic spinal tumor as one of the most useful treatment options and it has provided apparent improvement of axial mechanical pain for those patients via strengthening of vertebral body support.\(^{21}\)

VP using PMMA bone cement is a mechanical stabilizer of fractures.\(^{12}\) VP also has some benefit as a treatment option of metastatic spine lesion. It may have antitumor effect as a result of cytotoxicity and thermal effect.\(^{23-24}\) In addition, vertebral biopsies can be readily performed during these procedures if the etiology of vertebral abnormality is unclear or to confirm a suspected pathology.\(^{20}\) Many prospective\(^{25-30}\) and retrospective\(^{31-34}\) studies have reported apparent improvement of both pain score and functional outcome. We could also get statistically significant improvement after VP and consecutive radioisotope bone therapy.

Concerned about the possible complications of VP, some authors prefer to use balloon kyphoplasty. The reported range of radiologic extravasations in VP was 9.2–139% (multiple areas of extravasations occurred per level), whereas the range was 0–26.3% in kyphoplasty. The reported range of symptomatic extravasations in VP was 0–13.5%, while there were none in kyphoplasty.\(^{25-30,35-40}\) Although cement leakage is more frequent in VP than in kyphoplasty in these reports, symptomatic cement leakage is rare in the clinical setting. In our series, VP did not cause symptomatic cement leakage or other systemic complications.

As for the prophylactic use of VP, there is some argument in case of osteoporosis.\(^{41-43}\) However, prophylactic cement augmentation of vertebral body with metastatic lesion without fracture is worthwhile to relieve axial pain and improve the patient’s quality of life.

### Conclusion

According to our data, spinal stabilization using VP in patients with widespread bone metastases and impending cord compression is an effective way to decrease disability with pain and to facilitate subsequent systemic palliation of painful skeletal metastases by administration of Sm-153 EDTMP.

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