Pain Relief Associated with Radiotherapy for Symptomatic Vertebral Lesions in Multiple Myeloma- A Retrospective Analysis

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ABSTRACT

Introduction: Multiple Myeloma is the most common Plasma cell disorder in India. It is primarily involving the Bone Marrow and so most patients have lytic bone lesions. It is a systemic disease and chemotherapy is the primary treatment. However, as the disease involves the bone marrow or bone, lesions may progress and cause bone pain, fractures, spinal cord/nerve compression, and may be associated with soft-tissue masses posing a higher risk to patients. These local lesions require more local therapy such as surgical excision and/or radiotherapy for symptomatic relief and/or to prevent further local progression.

Radiotherapy (RT) alone is a definitive treatment choice for Solitary Plasmacytoma where moderate doses of radiation are good enough for cure (5). Radiotherapy has also an important role in the management of multiple myeloma by reducing painful osteolytic process and improving recalcification. Radiotherapy prevents pathologic fractures, prevents impending paraplegia, controls serious bone pain and reduces analgesic usage.

Objective

To assess the pain relief associated with palliative radiotherapy for Symptomatic Vertebral Lesions in Multiple Myeloma.

Materials and Method: After getting ethical clearance all patients registered in Radiotherapy department during the period January 2017 to December 2019 for THREE years with diagnosis of Multiple Myeloma and having vertebral lesion were enrolled for the study. The osteolytic vertebral lesion must be confirmed by X-ray or CAT scan or MRI evaluation as the case may be. All radiological assessments should have been done prior to the Radiotherapy

treatment. Radiation treatment was delivered using Linear Accelerator Varian Clinac IX with Megavoltage beams and appropriate Photon energy.

Numerical Pain Rating Pain Scale (NPRS) was used for pain level evaluation (7). A pain score ≤ 4 was classified as mild, 5-7 as moderate and severe if the pain score was ≥ 8 . All patients were evaluated in terms of their pain intensity before Radiotherapy (called as basal pain score) by using NPRS and they were re-evaluated 30-45 days after their radiation treatment by using NPRS.

Result: A total of 95 patients who fulfilled the inclusion criteria were enrolled in the study. Of the 95 patients there were 54 males and 41 females in the ratio 1.31: 1. One male patient had cervical and thoracic vertebral lesions and the Radiation treatment could not be completed because of his deteriorating performance status and was excluded from the study.

There were 102 vertebral segments of which 2 were excluded. The remaining 100 vertebral segments were Cervical 7, Thoracic 45, and Lumbosacral 48.

The main symptom was pain which was present in all the patients. Neurological symptoms such as Paresthesia, difficulty to walk, weakness of lower limbs were seen in 34 (36.17%) patients. It was noted that 4 (4.25%) patients had paraspinal soft tissue component as noted in the radiological investigation.

Numerical Pain Rating Pain Scale (NPRS) was used for pain level evaluation in 94 patients. Number of patients with No to Mild pain was 0; patients with moderate pain score was 4 (4.26%); and patients with severe pain score was 90 (95.74%).

After Radiation treatment, pain was reassessed using NPRS and it was found that patients with

Mild to No pain was 90 (95.74%); patients with moderate pain score was 3 (3.2%); and patients with severe pain score was 1 (1.06%).

Using the paired student T-test statistical analysis on Excel sheet it was found that the Mean Difference was -6.4, Standard deviation 1.607 which gave a highly significant p value <0.0001.

Patient who got more than 5 point reduction in NPRS scale was 89 (94.68%) and those with less than 5 point reduction in pain scale was 4 (4.26%). 1 (1.06%) had progressive weakness of lower limbs and had to undergo spine fixation surgery.

Conclusion: Radiotherapy is an excellent modality of treatment for significant pain reduction in patients having symptomatic vertebral lesion in Multiple Myeloma. It was noticed that most of the patients post RT required nil to minimum analgesics for pain relief. Although the pain relief in patients who had paraspinal soft tissue component was not much as the other patients.

Key Words: Multiple Myeloma, Palliative Radiotherapy, Numerical Pain Rating Scale (NPRS)

INTRODUCTION

Multiple Myeloma is the most common Plasma cell disorder in India. It is primarily involving the Bone Marrow and so most patients have lytic bone lesions. It is a systemic disease and chemotherapy is the primary treatment. However, as the disease involves the bone marrow or bone, lesions may progress and cause bone pain, fractures, spinal cord/nerve compression, and may be associated with soft-tissue masses posing a higher risk to patients. These local lesions require more local therapy such as surgical excision and/or radiotherapy for symptomatic relief and/or to prevent further local progression. These patients usually require immediate treatment relieve these painful to symptoms. However, systemic chemotherapy does not provide prompt symptom relief; thus, local treatment is necessary.

Radiotherapy (RT) alone is a definitive treatment choice for Solitary Plasmacytoma where moderate doses of radiation are good enough for cure. Radiotherapy has also an important role in the management of multiple myeloma by reducing painful osteolytic process and improving recalcification. Radiotherapy prevents pathologic fractures, prevents impending paraplegia, controls serious bone pain and reduces analgesic usage. Moreover, ensuring bone remodulation of lytic bone lesions caused by malignant tumor infiltration is accepted as a secondary and long term effect of Radiotherapy for this group of patient.

Chow et al. in the systematic review analysed 16 randomised trials comparing single fraction versus multiple fraction for bone metastases: no significant difference was found regarding response rates. An increased risk for pathological fractures and spinal cord compressions was observed in the SF regimen, which was statistically insignificant, while retreatment in the single fraction regimen was 2.5-fold higher. The role of different palliative radiotherapy regimens for multiple myeloma is not well established due to lack of clinical trials. Medical literature provides only a small number of studies dealing with various radiotherapy regimens for the treatment of patients with multiple myeloma as well as impact of the radiotherapy regimen on pain relief at the sites of bone destructions. However. final recommendations concerning the choice of the radiation therapy regime have not been presented yet.

The performance of cancer patients is assessed using the Eastern Cooperative Oncology Group (ECOG). To conduct clinical trials for the treatment of cancer in a consistent manner across many participating hospitals, cancer centers, and clinics requires the use of standard criteria for measuring how the disease impacts a patient's daily living abilities (known to physicians and researchers as a patient's performance status). The ECOG Scale of Performance Status is one such measurement. It describes a patient's level of functioning in terms of their ability to

care for them self, daily activity, and physical ability (walking, working, etc.).

MATERIALS AND METHODS

After getting ethical clearance all registered Radiotherapy patients in department during the period January 2017 to December 2019 for THREE years with diagnosis of Multiple Myeloma and having vertebral lesion will be enrolled for the study. The Case Registry file of all such patients will be retrieved from the cancer registry and details will be entered in separate proforma. The osteolytic vertebral lesion must be confirmed by X-ray or CAT scan or MRI evaluation as the case may be. All radiological assessments should have been done prior to the Radiotherapy treatment.

Radiation treatment was delivered using Linear Accelerator Varian Clinac IX with Megavoltage beams and appropriate Photon energy. Gross tumour volume (GTV) was to include the osteolytic vertebral lesion and the involved soft tissue. Clinical target volume (CTV) would include GTV plus potential area of involved microscopic disease site. The treatment is optimized to the Planned Target volume (PTV) which includes CTV plus 1cm margin all around. Dose delivered to the PTV by 3D Conformal Radiotherapy was 20Gy in 5 fractions or 30 Gy in 10 fraction. All radiation treatment was delivered 5 fraction per week.

Numerical Pain Rating Pain Scale (NPRS) was used for pain level evaluation. A pain score ≤ 4 was classified as mild, 5-7 as moderate and severe if the pain score was ≥ 8 . All patients were evaluated in terms of their pain intensity before Radiotherapy (called as basal pain score) by using NPRS and they were re-evaluated 30-45 days after their radiation treatment by using NPRS, as well. The pain response rate was defined according to the international consensus on palliative RT criteria.



The Numerical Pain Rating Scale (NPRS) is a subjective measure in which individuals rate their pain on an eleven-point numerical scale. The scale is composed of 0 (no pain at all) to 10 (worst imaginable pain).

Eastern Cooperative Oncology Group (ECOG)

GRADE	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light
	house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking
	hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair
5	Dead

Diagnostic criteria

In 2003, the International Myeloma Group (IMG) agreed on diagnostic criteria for symptomatic myeloma, asymptomatic myeloma, and MGUS, which was subsequently updated in 2009.

- Symptomatic myeloma (all three criteria must be met):
 - 1. Clonal plasma cells >10% on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (Plasmacytoma)
 - 2. A monoclonal protein (myeloma protein) in either serum or urine (except in cases of true nonsecretory myeloma)
 - 3. Evidence of end-organ damage felt related to the plasma cell disorder (related organ or tissue impairment, CRAB):
 - Hypercalcemia (corrected calcium >2.75 mmol/l, >11 mg/dl)
 - Kidney insufficiency attributable to myeloma
 - Anemia (hemoglobin <10 g/dl)
 - Bone lesions (lytic lesions or osteoporosis with compression fractures)

INCLUSION CRITERIA

All patients diagnosed with Multiple Myeloma with Vertebral lesion diagnosed using International Myeloma Group criteria. Eastern Cooperative Oncology Group (ECOG) performance scale 0 to 2

EXCLUSION CRITERIA

Eastern Cooperative Oncology Group (ECOG) performance scale 3 to 5 Prior Radiotherapy to vertebra same site Patient started on chemotherapy If surgical fixation done

RESULT

A total of 95 patients who fulfilled the inclusion criteria were enrolled in the study. Of the 95 patients there were 54 males and 41 females in the ratio 1.31: 1. The median age of the patients was 62 years (range 35 to 80 years). One male patient had cervical and thoracic vertebral lesions and the Radiation treatment could not be completed because of his deteriorating performance status and was excluded from the study.

There were 102 vertebral segments of which one patient who had 2 lesions in the cervical and thoracic vertebrae were excluded. The remaining 100 vertebral segments were Cervical 7, Thoracic 45, and Lumbosacral 48.

The main symptom for all the patients was pain. Neurological symptoms such as Paresthesia, difficulty to walk, weakness of lower limbs were seen in 34 (36.17%) patients. It was noted that 4 (4.26%) patients had paraspinal soft tissue component as noted in the radiological investigation.

Numerical Pain Rating Pain Scale (NPRS) was used for pain level evaluation in 94 patients. Number of patients with Mild to No pain was 0; patients with moderate pain score was 4 (4.26%); and patients with severe pain score was 90 (95.74%).





After Radiation treatment was given pain was reassessed using NPRS and it was found that patients with No to Mild pain were 90 (95.74%); patients with moderate pain score was 3 (3.2%); and patients with severe pain score was 1 (1.06%).



Using the paired student T-test statistical analysis on Excel sheet it was found that the Mean Difference was -6.4, Standard deviation 1.607 which gave a highly significant p value <0.0001.





Patient who got more than 5 point reduction in NPRS scale was 89 (94.68%) and those with less than 5 point reduction in pain scale was only 4 (4.26%). One patient had progressive weakness of lower limbs and was referred to Spine Neurosurgery department and underwent fixation surgery.

DISCUSSION

In our study of 94 patients with symptomatic vertebral lesion with diagnosis of Multiple Myeloma, we found that there was a slight male preponderance with ratio of 1.31: 1. This was comparable with the study by Daniel Mark et al.

Our study had mainly taken into consideration the pain associated with the vertebral lesion due to multiple myeloma and the pain relief that was associated with the delivery of palliative radiation treatment to involved vertebrae. The numerical pain rating scale was used for this assessment. We could observe a statistically significant reduction in the pain scale in the post radiotherapy patients when compared to the pre radiation group. Several studies like Leigh BR et al, Talamo G et al defined the response to radiotherapy as an improvement in subjective symptoms or performance status or a decrease in the use of analgesics.

These studies considered both complete and partial remission of symptoms when evaluating response. In those studies, symptom relief was reported in more than 80% of patients, and the radiation dose had no influence on in-field failure free survival.

In our study we observed a >5 point reduction in NPRS in 94.68% of patients. Neurological symptoms such as Paresthesia, difficulty to walk, weakness of lower limbs were seen in 36.17% patients. In the study done by Daniel Mark et al out of 54 patients he found symptomatic response as measured by a decrease of \leq 5 points on the pain related scale was 83% and 34% of patients had a decrease of >5 points. Of 35% of patients that had neurologic impairments prior to treatment, improvement was identified 83% of the time.

CONCLUSION

Radiotherapy is an excellent modality of treatment for significant pain reduction in patients having symptomatic vertebral lesion in Multiple Myeloma. It was noticed that most of the patients post RT required nil to minimum analgesics for pain relief. Although the pain relief in patients who had paraspinal soft tissue component was not much as the other patients. This could indicate the use of higher dose of Radiotherapy in this sub group of patients.

Conflict of Interest

Authors have declared no conflicts of interest

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