Role of Radiotherapy in Pain Palliation in Metastatic Bone Cancer: A Prospective Study

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Research Article

Abstract: Metastatic bone cancers frequently need pain palliation for which Palliative Radiotherapy remains mainstay. Bone metastasis is stage IV cancer and the patients have few months of remainder life and they have distressing symptoms. Objective of this study is to evaluate efficacy of radiotherapy in pain palliation to improve the quality of life with negligible side effects .A total of 38 patients were given palliative RT 30Gy/10 fractions by telecobalt machine and observations were done. Bone is a preferred site to metastasize by few malignant tumours (osteotropic) like breast, prostate, kidney, lung, GIT, thyroid. Other primary tumours giving metastases to bones are myeloma (plasma cell tumours), ovarian tumours, cervix, unknown primary cancers mostly anaplastic variety Metastatic bone disease is regarded as Stage IV disease which eventually affects the quality of life because of disabling skeletal related events, which usually are the consequences of advanced cancers.

1. Maximum number of patients were 40 to 70 years of age only 3 cases were above 70 years and 2 case were below 20 years of age .
2. Male patients outnumbered female patients.
3. Breast prostate lung cervix and myeloma cases were almost equal in number only two cases of Ewing's sarcoma below 20 years of age.
4. Axial skeletal involvement outnumbered the Appendicular skeleton.
5. Lytic bone lesions were more than mixed (Blastic and Lytic) lesions.

Keywords: Radiotherapy, Pain palliation, Hypo fractionated radiotherapy

Introduction

"Cancer" is a common term used for all kinds of malignant neoplasms, which may be regarded as a group of diseases characterized by an abnormal and uncontrolled growth of cells, which has ability to invade adjacent tissues and spread to distant organs and bones. Bone is a preferred site to metastasize by few malignant tumours (osteotropic) like breast, prostate, kidney, lung, GIT, thyroid. Other primary tumours giving metastases to bones are myeloma (plasma cell tumours), ovarian tumours, cervix, unknown primary cancers mostly anaplastic variety.[1, 2] Metastatic bone disease is regarded as Stage IV disease which eventually affects the quality of life because of disabling skeletal related events, which usually are the consequences of advanced cancers. According to GLOBOCAN 2012, an estimated 14.1 million new cancer cases and 8.2 million cancer-related deaths occurred in 2012.[5,30]

Magnitude of the problem of metastatic bone disease

Though there is availability of effective treatment with the help of radiotherapy and chemotherapy, patients with bone metastases have longer life than patients with visceral metastases.[6,7] This eventually gives distressing symptoms because of skeletal related events and affects the quality of life due to skeletal morbidity.[8] A major part of practice of oncology is concerned with pain palliation. There are various treatment modalities for pain palliation.[9] Among the available treatment modalities, radiotherapy since many decades, remains mainstay of the palliative treatment for bone metastases. More than 50% of the patients with the diagnosis of cancer receive radiotherapy as an adjuvant to surgery, chemotherapy or as a primary palliative treatment for metastatic lesions.[5, 10] considering the facts in the magnitude of the problem of metastatic bone disease, palliative treatment with radiotherapy since many decades was under evolution. The reasons were,

1. Relief from severe pain which was intended to give overall better quality of life, considering prolonged life.[9,11]
2. Metastatic bone disease becomes symptomatic earlier during its clinical course.[12]
3. High morbidity almost in one third of cases, because of skeletal related events and complications; patients need symptom palliation.[10]
4. Life expectancy of patients with bone metastases varies widely, with a survival between 7 to 19 months.

Bone only metastases without visceral metastasis of Ca. Breast have a 5 year survival rate of 45% with median

survival of 52 months. [13] Currently there is no standardized classification of patients with bone metastases, so .efforts are being made to develop such system for stratifying the patients for radiotherapy dose evaluation and comparison of results with prediction of patient's outcome.[11]

External beam radiotherapy

It is treatment by ionizing radiation (x-rays, gamma-rays, electron beams, neutron beams etc). The radiation is delivered externally to the surface of body. With the advent of Cobalt-60 teletherapy it became easier to give palliative treatment to metastatic bone lesions and is cheapest of all. External radiation may be delivered by various techniques Metastatic bone disease occurs in about 80% cases of advanced malignancies.[3,4] This leads to compromised quality of remaining life due to distressing skeletal related events and symptoms, especially pain. So there was a dire need for symptom palliation with either of the modalities, of which, more than 50% of patients need radiotherapy for metastatic bone pain which are in use since many decades.[3]

Clinical Presentation

In patients with known primary cancers, during their clinical course, may develop bone pain, which is considered to be highly suggestive of bone metastases. Many patients may not present with bone pain but with skeletal related complications, such as signs of cord compression, which occurs in about 5-10% of spinal metastases.[22] Pathological fracture may present with mild to severe pain and impaired mobility in 10% to 15% cases. Other Local presentation like diffuse hard swelling (may or may not be present). Tenderness at single or multiple sites sometimes may be associated with crepitus and abnormal movements. This presentation is common in spinal metastases. Limping gait is many times seen in pelvic bone metastases, sometimes even with restricted movements at hip joint.[12] Local field therapy was commonly used in patients with breast and prostate bone secondaries (79%). Long, fractionation scheme used by 90% of radiation oncologists in 96% of cases with bone metastases while short fractionation scheme was used by 7% physicians in 4% cases. Most common schedule was 30 Gy x 10 used by 77% of physicians in 64% of cases[20].

Material and methods

38 patients were given radiation to single most painful skeletal metastatic lesion among multiple lesions. The study was conducted during the period of three years in the Department of Radiotherapy and Oncology, Government Medical College and Hospital, Aurangabad, on OPD basis.

Investigations

Patients who do not complain of pain were investigated in detail.

Hematological profile included: CBC

Blood biochemistry included: LFT, KFT, Serum calcium, blood glucose, serum tumor markers (when needed).Special investigations included (When needed) : Serum electrophoresis and urinary B.J. Proteins (multiple myeloma), bone marrow examination. FNAC of site involved

Imaging work up

X-ray chest, X-ray of pain sites, X-rays of suspected metastatic sites (all x-rays with detailed reporting). Necessary skeletal survey was done with special imaging techniques by using CT scan, MRI, ^{99m}Tc Bone scan (optional) Assessment of pain was done by using simple rupee-scale and McGill's pain score.[25] Local field irradiation to most painful sites, among the multiple skeletal lesions. Field size was confirmed on marker x-ray for adequate safety margins. Patients were treated by Radiation which was given in dose of 30Gy in 10 fractions and no prior hospitalization was needed.

Observations

1. Patient's pain relief started within 24 hours after first fraction of radiotherapy.
2. Initial pain score in 37% of the patients was severe (grade III) and agonizing (grade IV) 26% of the patients
3. Most of the patients were on NSAID analgesics and 14% were on opiate analgesics and most of the patients stop analgesics consumption after radiotherapy.
4. In first 48 hours partial response(PR) seen in 26% cases and complete responders(CR)were 63% and rest of the cases showed CR in a week.
5. At 6 month follow up 77% cases were in CR and rest of the cases was in PR.
6. Patients compliance for follow up was 100% in first 6 months and 85% at first year.
7. There were no toxicities seen like fractures, erythema and dermatitis, opportunistic infections.
8. Maximum number of patients were 40 to 70 years of age only 3 cases were above 70 years and 2 case were below 20 years of age .
9. Male patients outnumbered female patients .
10. Breast prostate lung cervix and myeloma cases were almost equal in number only two cases of Ewing's sarcoma below 20 years of age.
11. Axial skeletal involvement outnumbered the Appendicular skeleton.

12. Lytic bone lesions were more than mixed (Blastic and Lytic) lesions.
13. There was moderate to severe pain in 50% cases and agonizing pain in 50% cases.
14. Seven patients had impending pathological fracture.
15. Nine patients had impending spinal cord compression.
16. At one year about 60% patients came for follow up and who did not come were considered dead.

Discussion

Palliative Radiotherapy is frequently needed for metastatic bone cancer patients for relieving distressing symptom pain which is moderate to severe grade sometimes agonizing too.Various dose fractionation schedules are in use since long time.[5] Pain relief is equally achievable even by single fraction schedules. Among them more popular schedules are 4Gy , 8Gy ,6Gy.[15] Partial pain relief starts within first 24 hours after first fraction and almost complete pain relief after course of Radiotherapy gets over, which lasts for longer duration.[1,5] Since involved field is given palliative radiotherapy there is no radiation induced toxicity observed. Sometimes multiple sites were to be treated for symptom palliation by planning at different sites. Multifraction Radiotherapy is inconvenient to the Patients. Hypo fractionationation Radiotherapy remains mainstay for symptom palliating of metastatic bone cancers. Considering the facts in the magnitude of the problem of metastatic bone disease, palliative treatment with radiotherapy since many decades was under evolution. The reasons were, relief of severe pain which was intended to give overall better quality of life, considering prolonged life. and metastatic bone disease becomes symptomatic earlier during its clinical course.[13] High morbidity almost in one third of cases, because of skeletal related events and complications; hence patients need symptom palliation.[3] Life expectancy of patients with bone metastases varies widely, with a survival between 7 to 19 months. However median survival of patients with bone metastases from various primaries is as follows Prostate (29.3 months), breast (22.6 months), kidney (11.8 months) and lung (3.6 months). Approximately 20% of breast cancer patients with predominantly bone metastases without visceral metastases have a 5 year survival rate of 45% with median survival of 52 months.[18] Prostate cancer with bone metastases have average life of 43 months in hormone responders and 20 months in non responders.[13,14] Duration of survival varies inversely with extent of the disease on initial bone scan.[15] Taking into account the magnitude of the problem of bone metastases and "cost-effectiveness" of various treatment modalities for pain palliation in patients with metastatic bone disease, radiotherapy being cheapest of all modalities, it was under evolution and wide usage since long time.[2,20] Patients with multiple bone metastases already have distressing symptoms and skeletal related complications. So it was the sole objective to eliminate or to decrease the disabling symptoms. This was achieved by various radiotherapy schedules put forth by different co-workers in radiation oncology.[1,5,] Many of them have observed almost similar effects of multifraction and single fraction low dose radiotherapy schedules, of which single fraction low dose schedule showed good efficacy and convenience to the patient and treating centre.[13,16] The management of symptoms of metastatic bone disease may be radiotherapy alone or it may be a combination of different treatment modalities like :

Surgery and post operative radiotherapy.[21]
Radiotherapy and analgesic therapy.[22]
Radiotherapy and bisphosphonates.[23,24,27,28]
Radiotherapy, chemotherapy and hormone manipulation.[1,3,5, 13, 14] Recent trends are concurrent use of Zoledronic acid with palliative radiotherapy since itenhances the effect of radiotherapy for symptom palliation. RT in combination with zoledronate has significantly prolonged skeletal related event- free survival and of pain response compared with RT alone in the treatment metastatic bone disease.[27,28]Response was mentioned in terms of Complete response (CR), Partial response (PR).

Following was the response rate observed by earlier workers for local field radiotherapy Source Madsen E.L., (1983)[26]

Reference	No. of Pts on t/t	Schedule	Response (%)	Type of study
Vargh *et al* (1969)	1324-16	Gyx1	90%	Retrospective
Jensen and Roesdahi 1976)	104 3-7	Gyx1	85%	Prospective, assessed by
Penn (1976)	8-15	Gyx1	89%	Retrospective
		3Gyx 10	94%	
Hendricknon *et al*	86	9 Gyx1, 6 Gyx2	88%	Prospective assessment by Physician
		3 Gyx5, 2Gyx10		
Allen K.L. *et al* (1976)	110	5 Gyx2, 2.5Gyx8	77%	
		4 Gyx5		
		2 Gyx20, 5Gyx4	78%	

		2.5Gyx16		
		4 Gyx8, 6Gyx5	80%	
		4 Gyx10		
Qasim (1977)	315	8-10Gyx1	73%	Retrospective
		4Gyx5	74%	
LeBonrgeois and cosset (1977)	100	8 and 5 Gyx2	65%	
		6 and 5Gyx2		
Gilbert *et al* (1977)	158	2Gyx15	73%	Retrospective Evaluation Method unclear
		2Gyx20		
		4Gyx5		
		6,5Gyx2 ±		
Ambard (1978)	64	15Gyx1	100%	Retrospective
Garmatis and Chu(1978)	75	2,5Gyx8	96%	Retrospective
		2,5 Gyx10		

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