

Analysis and treatment results of spinal Metastases; ten years experience of Alexandria clinical oncology department

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ABSTRACT

Background: This study attempted to review the medical records of all patients with spinal bone metastases presented to Alexandria Clinical Oncology and Nuclear Medicine Department (ACOD), Alexandria Main University Hospital during the period from January 2003 to December 2012.

Patients and Methods: A total of 350 patients were included in this study. Medical records were retrospectively reviewed and data were collected as regard demographic data, medical history, Clinical data, Investigations and diagnostic work up, treatment modalities and treatment outcomes.

Results: we observed that the origin of the tumor in the majority of cases was breast cancer (31.1%), followed by prostate cancer 17.7% then multiple myeloma 17.1%. The female patients presented with the highest percentage 60.9%. performance status according Eastern Cooperative Oncology Group (ECOG) score was 0-2 in 58% of patients. The majority of patients were complaining of pain (98.6%). A considerable percentage of cases presented with symptoms of spinal cord compression (30%). Improvement regarding pain after treatment with radiotherapy was reported in (42.6%) of patients. Motor function improvement was (89.7%) at 8 weeks for patients presented with paresis and treated early. Type of primary tumor was the most significant prognostic factor (HR=6.873 and 4.431, P <0.001).

Conclusions: Breast cancer, prostate cancer and multiple myeloma constituted the most common primaries that develop spinal metastases. A higher incidence of spinal metastases in women compared with men. The predominant symptom in patients with spinal metastases was pain. Patients who developed spinal metastases were at risk of spinal cord compression. The goals of treatment were to relieve pain and prevent complications. External beam radiotherapy has been the mainstay for palliating pain resulting from spinal metastases. Early initiation of radiotherapy promote better functional outcome. Type of primary tumor was identified as the most powerful prognostic factor for patients with spinal metastases.

Key Words: Spinal metastases, clinical oncology, breast cancer, prostate cancer and multiple myeloma.

INTRODUCTION

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Spinal metastasis represents an ominous extension of neoplastic disease.⁽¹⁾ Spinal secondaries comprise the

most frequently encountered spinal tumors and occur 20 times more often than primary neoplasms of the spine. Spinal metastases can affect up to 50% cancer patients.⁽²⁾ Spinal metastasis develops in all age groups; the highest incidence occurs during midlife (40–70 years of age), corresponding to the period of increased cancer risk. A somewhat higher incidence of spinal metastasis in men compared with women parallels the incidence of

prostatic versus breast carcinoma.⁽³⁾ tumors of the breast, prostate, lung and kidney constitute the most common culpable primaries, reflecting the prevalence and tendency for these tumors to metastasize to bone.⁽⁴⁾ The primary lesion remains unknown in 12.5 % of cases.⁽⁵⁾ Metastatic involvement of the spine arises in the thoracic region in 70% of the cases followed by the lumbar 22% and then the cervical spine 8%.⁽⁶⁾

Symptoms and signs: Local pain is the most common manifestation, occurring in 90% of the patients.^(6,7) Spinal tumor pain can present as slowly progressive continuous localized back pain, radicular pain or mechanical pain.⁽⁶⁾ Pain is associated with neurologic dysfunction in only 5% of cases. These patients are at risk of developing symptomatic spinal cord compression. Motor deficits are ranging 35–75% in metastatic spine patients at presentation.⁽⁸⁾ Sensory deficit often accompany the motor ones. Sphincter control is frequently preserved at the initial stages of the disease.⁽⁸⁾

Materials and Methods

Diagnostic evaluation: Laboratory studies:

Tumor markers as carcinoembryonic antigen (CEA), the prostatic specific antigen (PSA) and CA 15,3.^(8,9)

Several imaging modalities of varying sensitivity are helpful in identifying bony metastases including:

Plain x-rays, Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Bone scintigraphy.⁽¹⁰⁾

Biopsy:

Either open or percutaneous vertebral biopsy can be performed.

Treatment

Classification:

Numerous classifications have been proposed to describe the clinical presentation and results of treatment for patients with spinal metastases.⁽¹¹⁾ According to these classification systems, it is possible to formulate guidelines for the treatment corresponding to patient condition and estimated length of survival. The most recently introduced is Tokuhashi scoring system.⁽¹²⁾

Treatment modalities

Medical treatment including:

Steroids, radiation therapy, chemotherapy, hormonal treatment and Bisphosphonates.

Steroids: In acute neurologic deterioration, the use of steroids has been shown to be effective in stabilizing and sometimes reversing neurologic dysfunction.⁽¹³⁾

Radiation therapy: A variety of fractionation schemes are used for the radiotherapy of spinal metastases depending on the patient's clinical manifestations, prognosis and the goals of treatment.⁽¹⁴⁾

Chemotherapy and hormonal therapy: The long-term control of spine metastases entails systemic chemotherapy.⁽¹⁵⁾ Typically, hormonal drugs are used for prostate and breast metastases.⁽¹⁶⁾

Bisphosphonates: They are used as co-analgesics in cases of moderate and severe bone pain and can reduce the frequency of skeletal-related events.⁽¹⁶⁾

Operative treatment:

Different surgical techniques are used including: Percutaneous Vertebroplasty, Decompressive Laminectomy, Tumor Resection and Spinal Stabilization and realignment of spinal deformity.⁽¹⁷⁾

Patients and Methods

This study was a retrospective study which conducted on 350 patients with spinal bone metastases presented to Alexandria Clinical Oncology and Nuclear Medicine Department (ACOD), Alexandria Main University Hospital during the period from January 2003 to December 2012. The medical records of all patients included in this study were retrospectively reviewed and data were collected including: (1) patient's age, sex and residence. (2) confounding comorbidities. (3) family history. (4) presenting symptoms and signs. (5) documented pathological data. (6) diagnostic work up including: laboratory investigations and radiological investigations. (7) treatment modalities and treatment outcomes.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using minimum, maximum, median, mean and standard deviation. Kaplan-Meier Survival curve was used for local control and overall survival. Cox regression was done for the significant relation with overall survival.

RESULTS

According to the reported data of the patients we found that female patients presented with higher percentage (60.9%) than male patients (39.1%) with male to female ratio 1: 1.55.

In our study, performance status according to ECOG score, 58% had score 0-2, 18 % had score 3-4 while data on score were incomplete in 24% of cases.

In our study, type of primary tumor was divided into three groups according to growth rate of primary disease: Slow growth (breast, prostate and MM), Moderate (CUP, NHL, HCC and Cancer body uterus) and Rapid (NSCLC and urinary bladder cancer). The highest percentage of the primary tumor was breast (31.1%), followed by prostate 17.7% and M.M. 17.1%.

In our study, the majority of patients were complaining of pain (98.6%) followed by neurological symptoms (weakness, heaviness or paralysis of limbs, hypohesia of affected areas and bladder or bowel

incontinence) in 43.7% while patient complains were unknown in 10.3%. These patients include 105 cases (30%) presented with symptoms of spinal cord compression. 52 cases (14.9%) presented with paresis; 39 cases of them received radiotherapy early (within 48 hours) while 13 cases received radiotherapy late (after 48 hours).

Regarding fractionation schedule the majority of the patients 89.1% received 3 Gray in 10 Fractions followed by 24.9% received 4 Gray in 5 fractions then 2.6% received 2.5 Gray in 12 fractions and the lowest percentage 1.7% received 8 Gray in 1 fraction taking into consideration that there were patients received more than one radiotherapy field with different fractionations schedule.

In our study, improvement regarding pain was documented in the highest percentage of patients (42.6%) while no data were documented in 30.0% of patients.

In our study, motor function improvement was (89.7%) for patients presented with paresis and treated early and (15.4%) for patients presented with paresis and treated late (p- value < 0.001) when observed at 8 weeks which was highly statistically significant.

Regarding toxicity from radiotherapy, nausea and vomiting were documented in 31.1%, abdominal pain in 30.3%, skin manifestations in 29.1%, diarrhea in 10.0% while laryngitis and esophagitis in 5.7% of cases. There were no documented data on side effect of radiotherapy in 55.7% of the patients.

Table-1. Distribution of the patients regarding sex, ECOG performance status, type of primary tumor, Fractionation schedule, Side effects of radiotherapy and Symptoms

	No.	%
Sex		
Male	137	39.1
Female	213	60.9
ECOG performance status		
0 – 2	203	58.0
3 – 4	63	18.0
Incomplete data	84	24.0
Type of primary tumor		
Slow (breast, prostate and MM)	231	66.0
Moderate (CUP, NHL, HCC and Cancer body uterus)	74	21.1
Rapid (NSCLC and urinary bladder cancer)	45	12.9
Fractionation schedule		
8 Gy x 1F	6	1.7
4 Gy x 5 F	87	24.9
3 Gy x 10 F	312	89.1
2.5 Gy x 12 F	9	2.6
Side effects of radiotherapy		
Nausea and vomiting	109	31.1
Abdominal pain	106	30.3
Diarrhea	35	10.0
Laryngitis and esophagitis	20	5.7
Skin manifestations	102	29.1

No data	195	55.7
Symptoms		
Pain	345	98.6
Neurological symptoms	153	43.7
Unknown	36	10.3

MM: Multiple myeloma
 CUP: carcinoma of unknown primary origin
 NSCLC: Non-Small cell lung cancer
 HCC: Hepatocellular carcinoma
 NHL: Non-Hodgkin's lymphoma
 N.B. these patients include 105 cases (30%) presented with symptoms of spinal cord compression.

In our multivariate analysis of prognostic factors for survival, the type of primary tumor (HR=6.873 and 4.431, P <0.001)., ECOG performance status 3-4(HR=2.870,P <0.001), female patients (HR=3.096,P <0.001) and cord compression (HR=2.035 , P= 0.007) were significant prognostic factors. The type of primary tumor was the most significant prognostic factor.

Table-2. Multivariate analysis COX regression for overall survival

	Hazard ratio	95%CI	p
Type of cancer			
Slow			
Moderate	4.431	2.2-8.8	<0.001*
Rapid	6.873	3.9 – 12.1	<0.001*
Sex			
Male			
Female	3.096	1.9 – 5.1	<0.001*
Cord compression			
No			
Yes	2.035	1.2 – 3.4	0.007*
ECOG			
0 – 2			
3 – 4	2.870	1.7 – 4.8	<0.001*

CI : Confidence interval
 *: Statistically significant at p ≤ 0.05

DISCUSSION

The current study revealed that female patients presented with higher percentage 60.9% than male patients 39.1% with male to female ratio 1:1.55 which may be explained by the highest number of breast cancer as a tumor origin (31.1%) in patients presented to our department. This is in contrary to Zaikova et al.,⁽¹⁸⁾ Gasbarrini et al.⁽¹⁹⁾ studies in which the highest percentage of patients (60%) were males. Also in contrary to Harel et al.⁽²⁰⁾ who reported that the incidence of spinal metastasis is comparatively higher in males than in females probably because of higher incidence of prostate cancer relative to breast cancer.

In our study, performance status according to ECOG score, 58% had score 0-2, 18 % had score 3-4 while

data on score were incomplete in 24% of cases. This was in consistent with Rades et al.⁽²¹⁾ who reported that ECOG scores were 1-2 in 52% of the patients while Scores were 3-4 in 48% of the patients.

In agree with Papastefanou et al.⁽²²⁾ and Botterel et al.,⁽²³⁾ the highest percentage of the origin of the tumor was breast (31.1%), followed by prostate 17.7% and M.M. 17.1% in the present study, reflecting the prevalence and tendency for these tumors to metastasize to bone.

As reported by Georgy et al.⁽²⁴⁾ and Vander linden et al.,⁽⁴⁾ Pain was documented in the majority of patients (98.6%). Following pain, neurological symptoms (weakness, heaviness or paralysis of limbs, hypohesia of affected areas and bladder or bowel incontinence) were seen in 43.7% of patients in the current study.

In the current study, it is found that (30%) of the patients presented with symptoms of spinal cord compression including back pain, numbness in toes, fingers or buttocks, decreased sensation below the level of compression, weakness or paralysis of limbs below the level of compression, urinary and fecal incontinence).

Bach et al.⁽⁷⁾ studied the occurrence, symptoms and clinical presentation of spinal cord compression in 398 patients. They reported that these patients accounted for (61%) of the cases which presented by back pain, deterioration of gait and bladder dysfunction. This discrepancy was explained by the fact that cancer patients are living longer as a result of improved therapies with consequent long-term complications such as spinal cord compression.

In agree with Yang et al.⁽²⁵⁾ and Paholpak et al.,⁽²⁶⁾ thoracic vertebrae were the site of metastasis in the majority of cases (83.1%) followed by lumbo-sacral then cervical vertebrae (35.7% and 13.4% respectively) taking into consideration that there were patients received more than one radiotherapy field.

Regarding fractionation schedule, the majority of the patients 89.1% received 3 Gray in 10 Fractions followed by 24.9% received 4 Gray in 5 fractions then 2.6% received 2.5 Gray in 12 fractions and the lowest percentage 1.7% received 8 Gray in 1 fraction taking into consideration that there were patients received more than one radiotherapy field with different fractionations schedule.

Hartsell et al.⁽²⁷⁾ reported the results of randomized trial of palliative radiation therapy (RT) for osseous metastases study 9714 (Radiation Therapy Oncology Group (RTOG) 9714), they studied long course RT (30Gy/10 F) versus short course RT (8Gy/1F) in patients with vertebral body metastases in their subset analysis. No differences were found in terms of pain relief (62% for 30 Gy/10 F and 70% for 8 Gy/1 F; P-value = 0.59).

Regarding toxicity from radiotherapy, nausea and vomiting were documented in 31.1%, abdominal pain in 30.3%, skin manifestations in 29.1%, diarrhea in 10.0% while laryngitis and esophagitis in 5.7% of cases. There were no documented data on side effect of radiotherapy in 55.7% of the patients.

This found to be consistent with the results reported by Hartsell et al.⁽²⁷⁾ who reported that the most common toxicity was gastrointestinal toxicity but significant differences in acute toxicity (20% and 10% for 30 Gy/10 F and 8 Gy/1 F, respectively; P=0.01) and acute gastrointestinal toxicity (14% and 6%, respectively; P=0.01) were observed at 3 months.

In our study, Improvement regarding pain after treatment with radiotherapy (local pain control) was documented in the highest percentage of patients (42.6%) while no data were documented in 30.0% of patients. Zaikova et al.⁽²⁸⁾ evaluated pain in patients with spinal metastatic disease undergoing radiotherapy with supportive treatment and reported that radiotherapy is an important tool in the control of pain in patients with spinal metastatic disease.

In consistent with Bach et al.,⁽⁷⁾ motor function improvement was (89.7%) for patients presented with paresis and treated early and (15.4%) for patients presented with paresis and treated late. They were observed at 8 weeks. The relation between time to start treatment and outcome was highly statistically significant (p-value < 0.001).

In our multivariate analysis of prognostic factors for survival, the type of primary tumor was the most significant prognostic factor (HR=6.873 and 4.431, P < 0.001). This found to be in consistent with Kataoka et al.⁽²⁹⁾ who studied prognostic factors for survival in patients with spinal metastases. The type of primary tumor was identified as the most powerful prognostic factor for patients with spinal metastases (HR=6.80 and 1.80, P < 0.001).

CONCLUSIONS

Breast cancer, prostate cancer and multiple myeloma constituted the most common primaries that develop spinal metastases. A higher incidence of spinal metastases in women compared with men. The predominant symptom in patients with spinal metastases was pain followed by neurological symptoms. Patients who developed spinal metastases were at risk of spinal cord compression. There are several prognostic factors for survival in patients with spinal metastases including the type of primary tumor, gender, performance status and cord compression. The most powerful prognostic factor is the type of primary tumor. The goals of treatment were to relieve pain and prevent complications so improve quality of life and overall survival of patients with spine metastases. External beam radiotherapy has been the mainstay treatment for palliating pain resulting from spinal metastases. Early initiation of radiotherapy promote better functional outcome in patients presented with paresis.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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