



CLINICAL PROFILE AND SURVIVAL ANALYSIS OF PATIENTS WITH BRAIN METASTASES TREATED BY PALLIATIVE WHOLE BRAIN RADIOTHERAPY

Upendra Nandwana¹, Naresh Jakhotia¹, TP Soni¹, Manoj Verma², R. K. Spartacus², Naresh Somani¹, Aseem Samar¹, Narendra Rathore³ and Sunnia Gupta³

¹BMCHRC, Rajasthan, India

²Department of Community medicine & family welfare AIIMS Jodhpur

³Department of Radiation Oncology Udaipur

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ABSTRACT

Introduction: Brain metastases are the most common type of intracranial neoplasm, with the total number outnumbering primary brain tumors by a ratio of 10:1 and occur in about 25% of cancer patients.

Aim: The purpose of this study was to analyze retrospectively the clinical profile and survival of patients with brain metastases.

Materials and Methods: This study analyzed a total of 130 patients with brain metastasis admitted from January 2012 to December 2016. Of these, 101 patients who received whole brain radiotherapy (WBRT) were included in this study. Prognostic factors evaluated for overall survival were age, gender, Eastern Cooperative Oncology Group (ECOG) score, primary histology, number of lesions, location of lesion, primary tumour site, extracranial metastasis. It is a retrospective, descriptive study.

Results: Brain metastases were more common in male and occur in 6th decade of life mostly. Carcinoma lung was the most common primary giving rise to brain metastases followed by breast. Adenocarcinoma accounts for most common histology of the primary that give rise to metastases. Multiple metastases were more common than the single one. Supratentorial lesions were more common than infratentorial lesion. The median overall survival was about 2 months while 1 year survival rate was 7%. In this study, patients with female gender, ductal and lobular as primary histology, solitary metastasis and carcinoma breast as primary had better survival.

Conclusions: Present study highlights that carcinoma lung accounts for majority of brain secondaries. Patients with solitary metastasis and carcinoma breast as primary tumor have comparatively better prognosis. Despite use of radiotherapy survival is poor. So efforts should be made for early diagnosis of brain metastasis in malignancy of other sites beside breast carcinoma and to incorporate multimodality treatment approaches including radiotherapy, radiosurgery, chemotherapy in treatment.

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INTRODUCTION

Brain metastases are the most common type of intracranial neoplasm, exceeding all other intracranial tumors combined.[1] They outnumber primary brain tumors by a ratio of 10:1 and occur in about 25% of all patients with cancer.[2] Brain metastases increases morbidity and mortality in cancer patients. An estimated 20% to 40% of all patients with metastatic cancer would have brain metastases at autopsy.[3]

Majority of patients who develop brain metastases have a known primary cancer (metachronous presentation).

*Corresponding author: **Upendra Nandwana**
BMCHRC, Rajasthan, India

primary site of cancer is detected in 5-10% of patients with brain metastases.[4] Brain metastases are located in the cerebral hemispheres in about 80%, in the cerebellum in 15% or in the brainstem in 5% of patients.[5]

In recent years, there has been apparent increase in cases of brain secondaries due to increasing incidence of lung cancer, improved detection by more sensitive imaging techniques, prolonged survival due to development in anticancer treatment.[6,7,8]

The clinical presentation of brain metastases is similar to any intracranial mass lesion and include headache (70%), seizures (30-60%), cognitive impairment (30%), papilledema (8%) and miscellaneous focal neurological deficits. [3,9]

Advances in neuroradiology have contributed greatly to the diagnosis and management of patients with suspected

neoplastic diseases of central nervous system (CNS). Contrast-enhanced computed tomography (CECT) and Contrast enhanced magnetic resonance imaging (MRI) are now widely used in detecting brain metastasis. [10,11,12]

The purpose of this study was to analyze the clinical profile and survival of patients with brain metastases.

MATERIALS AND METHODS

A retrospective study of medical records of 130 patients with brain metastasis was carried out at Bhagwaan Mahaveer Cancer Hospital and Research Institute. Patients admitted between January 2012 and December 2016 were included in the study. Of these 29 patients not willing for radiotherapy and chose only best supportive care were excluded from the study. Information was collected regarding history, clinical examination including neurological evaluation; fundoscopy and perimetry (in selected cases); complete blood count, liver and kidney function test; imaging - CT/MRI scan of the brain and other different imaging studies which were done to detect the primary and histopathological biopsy confirmation of the primary site. The survival times were considered as the time between diagnoses of brain metastasis and the last followup or recorded death. Prognostic factors evaluated for overall survival were age, gender, ECOG score, primary histology, number of lesions, location of lesion, primary tumour site, primary controlled or not and extracranial metastasis in patients treated with whole brain radiotherapy.

Statistical analysis: Categorical data was expressed proportion (%) and continuous data as mean (Standard deviation) and median. Categorical data was inferred using Chi square test. Survival analysis was done using Kaplan Maier curve and Cox regression analysis. Statistical analysis was performed using SPSS trial version 20.

RESULTS

There were 101 patients with brain metastases admitted between January 2012 and December 2016. Out of the total 101 patients with brain metastases 57(56.43%) were males and 44 (43.56%) were females.

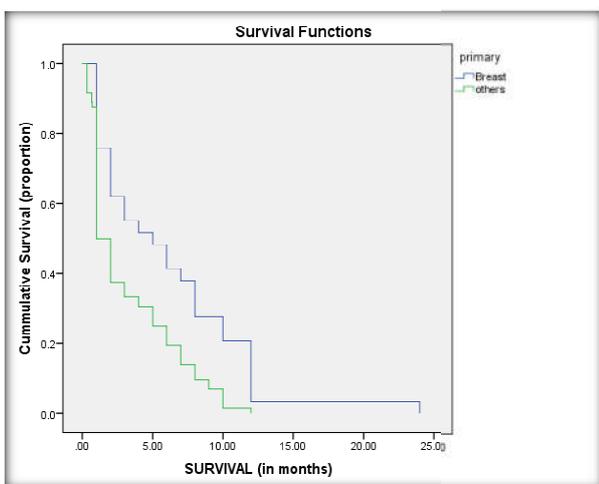


Fig 1 Kaplan-Meier survival curve for patients with brain metastasis undergoing WBRT plotted against the primary of the disease (breast v/s others)

In this study, 73 patients were below 60 years of age. Carcinoma of the lung was the commonest primary that

metastatizes to brain i.e. 51.48%, followed by breast (28.71%). In the majority of patients, histology of primary malignancy was adenocarcinoma constituting 38.61% followed by ductal and lobular histology in 28.71% and squamous cell carcinoma accounted for 10.89%of cases. In five percent of cases histology of the primary site was unknown. Supraratentorial brain metastasis was seen in 58(57.42%) patients while 10(9.90%) patients had infratentorial lesions. Out of 101 patients, 89(88.11%) had multiple lesions and 12(11.88%) had single lesion. Headache was the most common symptom followed by vomiting and weakness. At the time of detection of metastases, only one fourth of patients had controlled primary whereas in 3/4th of the patients, the primary disease was not controlled. All 101 patients were treated with WBRT along with dexamethasone, mannitol, and other supportive treatment. Patient characteristics are described in [Table 1].

Table 1 Characteristics of the patients

Primary tumor site	Number of cases	Percentage (%)	Survival at 1 year
Lung	52	51.48	1
Breast	29	28.71	6
Endometrium	2	1.98	0
Ovary	2	1.98	0
Choriocarcinoma	1	0.99	0
Prostate	1	0.99	0
Urinary Bladder	1	0.99	0
RCC	2	1.98	0
Oesophagus	2	1.98	0
Rectum	2	1.98	0
Sarcoma	1	0.99	0
Malignant melanoma	1	0.99	0
Unknown primary	5	4.95	0

Table 2 Univariate analysis of characteristics of patients

Variables	Number	Percentage	Number of pts with survival >1 year	P
Total patients	101	100	7(6.93)	
Sex				
Male	57	56.43	0	0.006
Female	44	43.56	7	
Age				
<60 years	73	72.27	3	0.172
>60 years	28	27.72	4	
ECOG performance score				
1-2	66	65.34	6	0.446
3-4	35	34.65	1	
Primary Histology				
Adeno	39	38.61	1	0.009
Squamous	11	10.89	0	
Ductal & Lobular	29	28.71	6	
Others	22	21.78	0	
Number of lesions				
Single	12	11.88	3	0.043
Multiple	89	88.11	4	
Location of lesion				
Cerebral	58	57.42	3	0.227
Cerebellar	10	9.90	2	
Both	33	32.67	2	
Primary tumour				
Controlled	25	24.75	2	0.833
Uncontrolled	76	75.24	5	
Extracranial metastasis				
Yes	50	49.50	3	0.978
No	51	50.49	4	
Site of Primary tumour				
Breast	29	28.71	6	<0.01
Others	72	71.28	1	

The median overall survival was 2 months (95% confidence interval [CI]: 1.247 - 2.753 months), and the 1-year survival rate was 7%. Those patients who had solitary brain metastasis ($P = 0.043$), female gender ($P=0.006$), ductal and lobular as primary histology ($P=0.009$) and breast carcinoma ($P<.01$) had significantly better survival [Table 2]. [Fig 1] shows Kaplan-Meier survival curve plotted against site of primary.

DISCUSSION

Brain metastasis is a significant cause of morbidity and mortality among cancer patient and its treatment is multidisciplinary with radiation forming the cornerstone of treatment.[13,14] In present study, nearly one third of patients were in the 6th decade and one fourth of patients were in 5th decade of life. Victor *et. al.*[15] reported that about 60% of patients of brain metastasis were aged between 50 and 70 years. In another study by Takokura *et al.* the age of onset of brain metastases was found to be 56 years in males and 40 years in females.[16]

In present study, brain metastasis occurred with almost equal distribution in male and female (56.43% vs. 43.56%). Victor *et.al.* [15] Similarly reported that the overall incidence of brain metastasis did not differ in both gender.

In this study, adenocarcinoma was found to be the most common histology of primary malignancy accounting for 38.61% of case, followed by Squamous cell carcinoma found in about 29% of cases. Histology of primary site was unknown in about 5% of cases. In a study, Debnath *et al.*[17] also reported adenocarcinoma (40.00%) as the commonest histology of the primary tumor followed by small cell carcinoma of lungs (28.57%) and squamous cell carcinoma (22.86%).

In the present study majority of cases (90%) had supratentorial lesion, and Parietal lobe was found to be the most common site of brain metastasis. Only 10% of cases had infratentorial involvement. This correlate with findings of other studies like Delattre *et al.*[2] and Nussbaum *et al.*[18] who reported cerebrum as most common site of brain metastasis and less commonly, cerebellum and brainstem.

In present study, most of the patients (88%) had multiple lesions and only 12% had single lesion. Similar finding was reported by Delattre *et al.* [2], were most cases majority of brain metastasis cases were reported to have multiple lesion on CT scan. Posner *et al.* [9] and Sze G *et al* [19] also reported multiple metastasis to be more common than single brain metastasis.

In present study, carcinoma of the lung was the most common primary that metastasizes to brain (51.48%), followed by carcinoma breast (28.71%). In 5% of patients, the primary was unknown. This finding correlates with other past studies. Lassman and De Angelis [20] in a review reported that the primary histology were mainly lung cancer (18-64%), breast cancer (2-21%), colorectal cancer (2-12%), melanoma (4-16%), etc and unknown primary in 1-18% of cases. In a study including 2700 subjects in New York, the most common primary reported were lung (48%) and breast (15%).[15] Takokura *et al.*[16] also reported carcinoma lung (48%) and carcinoma breast (25%) as most common primary in brain metastases patients.

Symptoms of brain metastasis are usually related to the location of the tumor, with most patients experiencing subacute symptoms only. In this study, Headache was the most common symptom in brain metastasis, experienced by more than half of patients followed by vomiting reported by about one fourth of cases. Neurological deficit was present in only 12% case and seizure in only 5% cases. Similar spectrum of symptoms in brain metastases have been reported by other studies. Posner *et al.*[9] reported headache as the most common symptom found in 49% of patients followed by mental changes (32%), focal weakness (30%) and seizures (18%). In yet another study, Victor [15] also found headache (42%) as most common symptom followed by seizure (21%) and cognitive dysfunction and motor dysfunction was found in nearly one third of patients.

In present study, at the time of detection of metastases, in two third of the patients, the primary disease was not controlled as was similarly found by Victor [15] *et.al.*

In present study solitary brain metastasis ($P = 0.043$), female gender ($P=0.006$), ductal and lobular as primary histology ($P=0.009$) and breast carcinoma ($P < 0.01$) were found to be significantly associated with better survival. Other studies like Borgelt B [21], Lang FF [22], Patchell RA [23], Schellinger PD [24] and Gasper LE [25], Ekici K [26], Manashi Ghosh [27] and Jakhar SL [28] have reported various prognostic factors associated with better survival include solitary metastasis, breast carcinoma, female sex, primary under control, good ECOG performance status.

CONCLUSION

Present study highlights that carcinoma lung accounts for majority of brain secondaries. Patients with solitary metastasis and carcinoma breast as primary tumor have comparatively better prognosis. Despite use of radiotherapy survival is poor. So efforts should be made for early diagnosis of brain metastasis in malignancy of other sites beside breast carcinoma and to incorporate multimodality treatment approaches including radiotherapy, radiosurgery, chemotherapy in treatment.

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