

Pattern of care and epidemiology of brain metastasis over past 10 years: A retrospective study from tertiary cancer center

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ABSTRACT

Background: In adults most common intracranial malignant lesion is brain metastasis, far outnumbering primary brain tumor. The most common primary site is lung cancer (18–64%), followed by breast (25–21%), malignant melanoma (4–16%), and colorectal cancer (2–12%). It is hypothesized that the incidence of brain metastasis might be increasing, as a result of increasing survival from recent advance in cancer treatment, more frequent brain screening for specific primary malignancy that known to have a higher prediction for brain metastasis and greater availability and use of magnetic resonance imaging (MRI) of brain. In clinical oncology, understanding brain metastasis is important, because it has profound effect on length of survival, quality of life, and in one-third to one-half of affected patients, they represent the direct cause of death despite current improvement in therapeutic approach. Epidemiological data of brain metastasis are lacking in India. **Objectives:** Aims of our retrospective analysis are to study epidemiology and pattern of care of brain metastasis over last one decade in Nil Ratan Sircar Medical College and Hospital, Kolkata. **Materials and Methods:** Between 2006 and December 2017, a total of 710 patients of brain metastasis treated in our department with palliative intent were analyzed retrospectively. New-onset neurological symptoms in a known case of cancer we always presumed that, symptoms were due to brain metastasis until proven otherwise. Hence, all patients presenting with acute neurological signs and symptoms underwent through clinical examination, contrast-enhanced (CE) computed tomography brain, and/or CEMRI of brain. Epidemiology, pattern of care, and outcome in the form of overall survival (OS) and disease-free survival were determined. **Results:** Fifty-seven percent patients were male. The median age was 62 years at the time of diagnosis. Lung carcinoma was most common primary site seen in 52% patients, followed by carcinoma breast second most common primary site, seen in 32% patients. Headache (73%) and motor weakness were most common presenting symptoms. Supratentorial location most common site, out of which parietal region is most common. The only small number of patients was offered best supportive care alone whereas majority of the patients were considered fit for palliative therapy. Treatment consisted of metastasectomy when possible and palliative whole-brain radiotherapy (WBRT) alone or followed by systemic therapy. Optimal supportive care in addition to chemotherapy or radiotherapy is given to all patients. A total of 254 patients were given blood product, erythropoietin, granulocyte-colony-stimulating factor following chemotherapy. Hospitalization required in 71% patients and tumor-related problem was most common cause (46%). Remaining patients were hospitalized for delivery WBRT or CCT.

The median OS is 9 months. Patients with younger age and breast primary associated with better prognosis than lung primary. **Conclusions:** We can conclude that carcinoma lung in male and carcinoma breast in females was most common cause of brain metastasis. Because advance in palliative therapy, outcome of patients with brain metastasis has improved, and patients with brain

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metastasis benefit from palliative radiotherapy and chemotherapy and this treatment could be delivered easily on outpatients basis.

KEY WORDS: Metastasis; Radiotherapy; Toxicity; Brain Metastasis

INTRODUCTION

Worldwide non-communicable disease (NCD) responsible for 63% death in the year 2008, and in India, NCD accounts for 53% of deaths. Among NCD, cancer one of the leading causes of death in India and accounts for 6% mortality in the year 2008.^[1] In adults most common intracranial malignant lesion is brain metastasis, far outnumbering primary brain tumor and it develops at a median time of 8.5–12 months from primary diagnosis of malignancy.^[2] In cases of melanoma, breast cancer, renal cell carcinoma (RCC), the median interval from diagnosis of cancer to that of brain metastasis is 2–3 years.^[2] Although brain metastasis can arise from any primary site, certain tumor has a predilection for brain metastasis, depending on site of primary and histological type. The most common primary site is lung cancer (18–64%) followed by breast (25–21%), malignant melanoma (4–16%), and colorectal cancer (2–12%).^[3-6] On the other hand, non-melanoma skin cancer, adenocarcinoma of prostate, squamous cell carcinoma of oropharynx, are least common primary site for brain metastasis. Most brain metastasis form solid tumor results from hematogenous spread rather than from dissemination through colony-stimulating factors (CSF) or direct brain invasion from head and neck malignancy. The incidence of brain metastasis is approximately 17,000–300,000 cases annually.^[2] It is hypothesized that the incidence of brain metastasis might be increasing, as a result of increasing survival from recent advance in cancer treatment, more frequent brain screening for specific primary malignancy that known to have a higher prediction for brain metastasis and greater availability and use of magnetic resonance imaging (MRI) of brain.^[2] In clinical oncology, understanding brain metastasis is important because it has profound effect on length of survival, quality of life, and in one-third to one-half of affected patients, they represent the direct cause of death despite current improvement in therapeutic approach. Epidemiological data of brain metastasis are lacking in India. With this context, we wanted to study epidemiology and pattern of care of brain metastasis in last one decade in our hospital Nil Ratan Sircar Medical College and Hospital, Kolkata.

MATERIALS AND METHODS

Between 2006 and December 2017, a total of 710 patients of brain metastasis treated in our department with palliative intent were analyzed retrospectively. From database age, sex, histology, primary site, and clinical features were collected.

New-onset neurological symptoms in a known case of cancer we always presumed that symptoms were due to brain metastasis until proven otherwise. Hence, all patients presenting with acute neurological signs and symptoms underwent through clinical examination, contrast-enhanced computed tomography (CECT) brain, and/or CEMRI of brain. Full systemic workup (CECT chest, whole abdomen pelvis, [fluorodeoxyglucose-positron emission tomography CT scan, bone scan when indicated]) promptly initiated if brain metastasis was presenting event to detect primary site and to rule out any other site of metastasis. Epidemiology, pattern of care, and outcome in the form of overall survival (OS), disease-free survival were determined. Despite the fact, that our study is a retrospective one and all the epidemiological and treatment related data have been collected from our own old records section of the Department of Radiotherapy of Nil Ratan Sircar Medical College and Hospital only, we have received formal permission from our Institutional Ethics Committee stating the nature of the study and that no harm and no financial burden would occur to the patients and that the further management of the patients will also not be affected by this retrospective analysis.

RESULTS

Patients' demographic profile is depicted in Table 1. Fifty-seven percent patients were male. The median age was 62 years at the time of diagnosis. Lung carcinoma was most

Table 1: Epidemiology of brain metastasis

Variables	Value
Primary site	
Lung	52%
Breast	32%
Malignant melanoma	8%
Renal cell carcinoma	6%
Colon	1%
Germ cell tumor	1%
Relevant facts	
Median survival	9 months
Age	
Median age	62 years
Range	29–86 years
Sex	
Male	57%
Female	43%

common primary site seen in 52% patients, followed by carcinoma breast second most common primary site, seen in 32% patients. Carcinoma colon and germ cell tumor was least common primary site. Headache (73%) and motor weakness were most common presenting symptoms [Table 2]. Supratentorial location most common site, out of which parietal region is most common. Cerebellum least common site, seen in <1% patients. Brain stem metastasis was not seen in our patient's cohort. Bilateral brain involvement was seen in 78% patients. Multiple brain lesions were seen in 91% patients. Treatments details are depicted Table 3. Only small number of patients was offered best supportive care alone whereas majority of the patients were considered fit for palliative therapy. Treatment consisted of metastasectomy when possible and palliative whole-brain radiotherapy (WBRT) alone or followed by systemic therapy. Platin doublet chemotherapy was the most common chemotherapy regimen in case lung primary. TAC or AC followed T combination and lapatinib or trastuzumab were used in the case of HER2 neu-positive breast primary. Surgical excision of solitary brain metastasis (metastasectomy) followed by WBRT possible in 14 patients (1%). Optimal supportive care in addition to chemotherapy or radiotherapy is given to all patients. Palliative RT to whole brain delivered by two parallel opposed fields in co⁶⁰ either 20Gy/5#/1 week, or 30Gy/10#/2 week. Concurrent chemoradiation for brain

metastasis not used at all because doubtful benefit. Total 254 were given blood product, erythropoietin, and granulocyte-CSF following chemotherapy. Hospitalization required in 71% patients and tumor-related problems was most common cause (46%). Remaining patients were hospitalized for delivery WBRT or CCT. Fourteen days were median duration of hospitalization range (2–31 days). The median overall survival (OS) is 9 months. Patients with younger age and breast primary associated with better prognosis than lung primary.

DISCUSSION

In our retrospective analysis, the most common primary site metastasizing to brain was lung carcinoma seen in 52% patients, followed by carcinoma breast second most common primary site, seen in 32% patients. Carcinoma colon and germ cell tumor was least common primary site. Headache (73%) and motor weakness (61%) were the most common presenting symptoms. The median overall survival (OS) is 9 months. Patients with younger age and breast primary associated with better prognosis than lung primary. Over 97% patients could be offered palliative radiotherapy and/or CCT, despite Eastern Cooperative Oncology Group (ECOG) status ≥ 2 in 18% patients and majority patient completed treatment with minimal toxicity. A significant proportion patient required multiple hospitalizations mostly due to tumor-related events.

Historical data showed that 10% patients diagnosed by CT scan or MRI brain were asymptomatic. Because screening scan is more frequently performed, a higher percentage of patients now presented with asymptomatic brain metastasis but can present with various symptoms; patient's quality of life can be affected significantly throughout course of disease and these symptoms are mostly related to intracranial location of metastasis; tumor or tumor-related edema or raised intracranial tension causing brain compression.^[2] In our study, 9% patients diagnosed in asymptomatic state and comparable to historical data. Headache (73%) and motor weakness (61%) were most common presenting symptoms in our study symptoms. In multiple published literature, lung carcinoma is most common primary site (20–50%) followed by breast (5–20%), small cell lung cancer (15%), melanoma (7–10%), and RCC (4–6%).^[2-4,7] In our study, lung carcinoma is the most common primary site (52%) followed by breast (32%), melanoma (8%), and RCC (6%) correlates with above studies. Nussbaum *et al.* and Delattre *et al.* reported approximately 80% of lesion found in supratentorial, 15% in cerebellum and 5% in brain stem.^[5,8] In our study, supratentorial metastasis is common site; seen in 83% patients followed by infratentorial metastasis (12%) and in 5% patients lesion seen in both supratentorial and infratentorial locations. In patients whose primary disease was not controlled, maximum number of brain metastasis seen in these groups of patients.^[9,10] In our present study, the primary disease was not controlled

Table 2: Clinical presentation of brain metastasis

Symptoms	%
Headache	73
Motor weakness	61
Mental disturbance	48
Convulsions/seizures	29
Cerebellar symptoms	18
Speech problem	23

Table 3: Treatment details

Variables	n (%)
Best supportive care only	29 (2)
Surgery plus WBRT	14 (1)
WBRT	
30Gy/10#/2 weeks	540 (76)
20Gy/5#/1 weeks	150 (21)
Chemotherapy regimen	
Paclitaxel plus carboplatin	156 (22)
TAC	220 (31)
Cisplatin plus etoposide	178 (25)
BEP	7 (1)
CAPOX	6 (1)
Temozolomide	6 (1)
Sunitinib	35 (5)
DTIC+platin	42 (6)

WBRT: Whole-brain radiotherapy

in 80% patients at the time of detection of metastasis, and in 20% patient's primary disease well controlled at the time of diagnosis of brain metastasis, correlated well with published literature. About 60% patients are aged between 50 and 70 years.^[3,9] In our study, median age at diagnosis is 62 years. In female, although melanoma spread to brain less common, overall incidence of brain metastasis does not affect by gender.^[11-13] In our study, there was almost equal distribution among males and females (57% vs. 43%). In our study, 98% of patients received radiotherapy and/or chemotherapy despite the ECOG status ≥ 2 , and majority patients tolerated the treatments with minimal toxicity. For the treatment of brain metastasis, palliative radiotherapy has been standard of care in most of the centers.^[14] Although multiple fractionation schedule has been reported, 30Gy in 10 fractions is most frequently used fractionation schedule in most of the centers. For patients with poor performance status and/or uncontrolled extracranial disease burden, shorter fractionation schedule, i.e., 20Gy in 5 fractions can be considered. This is because this fractionation schedule associated with higher radiological response and better quality of life.^[15,16] We have used this fractionation schedule in 76% patients and 20Gy in 5 fractions in 21% patients in our study. In patients with brain metastasis, the median OS ranges from 4 months to 12 months.^[17-20] The median overall survival (OS) is 9 months. Although a majority of patients with brain metastasis ultimately succumb to systemic progression, a significant percentage of patients will die from neurologic progression. To optimize brain control multiple randomized trials of concurrent radiosensitizers have been tried. However, no trial has demonstrated a survival advantage.^[21-28] That why we have not used concurrent radiosensitizers during WBRT in our study.

However, our results may not be true representative of all brain metastasis in patients' population from the community because it is retrospective and single-institution study.

CONCLUSIONS

We can conclude that carcinoma lung in male and carcinoma breast in females was most common cause of brain metastasis. Because advance in palliative therapy, outcome of patients with brain metastasis has improved and patients with brain metastasis benefit from palliative radiotherapy and chemotherapy and this treatment could be delivered easily on outpatients basis.

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