

EFFECTIVENESS OF RADIATION TREATMENT IN METASTATIC BRAIN DISEASESPrema K. R¹¹Associate Professor, Department of Radiotherapy, Government Medical College, Thrissur, Kerala, India.**ABSTRACT****BACKGROUND**

Brain metastasis are a major cause of mortality and morbidity in cancer patients. Most common primary sites are lung, breast, malignant melanoma and kidney. Whole brain radiation treatment has remained the treatment of choice for brain metastasis. Though it provides early symptomatic relief, survival is limited to 3-6 months.

AIM

To study the effect of radiation on relief of symptoms and on the survival of patients with brain metastasis, also analysing the incidence of brain metastasis from different primary sites.

METHODS

This study was conducted in Radiotherapy department of Government Medical College, Calicut during 1997-1999, involving 50 patients with radiologically proven brain metastasis. All patients received whole brain radiation treatment to a dose of 3000 cGy /10 F/2 weeks and were analysed for symptomatic relief and survival.

RESULT

About ¾th of the patients obtained symptomatic relief within 2 weeks after starting radiation treatment. 72% of patients survived upto 6 months after radiotherapy.

CONCLUSION

External beam irradiation to whole brain in the dose of 3000 cGy/10F/2 weeks is an effective method of treatment of brain metastasis both in terms of early symptomatic relief and survival.

KEYWORDS

Brain Metastasis, Radiotherapy, Survival.

HOW TO CITE THIS ARTICLE: Prema KR. Effectiveness of radiation treatment in metastatic brain diseases. J. Evid. Based Med. Healthc. 2016; 3(21), 882-884. DOI: 10.18410/jebmh/2016/200

INTRODUCTION: Brain is a favourable site of metastasis affecting about 25% -35% of all cancer patients.¹ The rising incidence of brain metastasis is most likely from a combination of increasing survival from recent advances in systemic therapy and a greater availability and use of MRI Scan. The occurrence of brain metastasis which often present dramatically and which carries a poor prognosis with survival limited to 3-6 months.²

The primary tumour site is most often lung (30-60%)^{3,4,5} and breast 13-21%. The other primary sites of metastasis to brain are melanoma, renal cell carcinoma, thyroid, seminoma and osteogenic sarcoma. Multiple metastasis are common in lung cancer, melanoma and breast cancers. Solitary metastasis are common in renal cell carcinoma. In some patients the primary tumour was undetectable when brain metastasis occurred.⁶ The presence of solitary or multiple metastatic deposits is clinically significant in selection of therapy, as surgical option is often limited to solitary metastasis.⁷ Whole brain radiotherapy has been

considered the standard treatment for brain metastasis.⁸ Now recently stereotactic surgery is also a therapeutic option for brain metastasis. Common prognostic factors for better survival are younger age (<65 years), Karnofsky performance score >70, good control of primary tumour, absence of extracranial metastasis.^{9,10} A total of 30 Gy in 10 fractions continues to be the most frequently employed fractionation schedule. Other fractionation schedules are 20 Gy in 4 fractions, 40 Gy in 20 fractions.¹¹ The short fractionation schedules such as 20 Gy in 4 fractions and 20 Gy in 5 fractions will produce late radiation toxicity if the patients live longer, so it is avoided in patients with good prognostic factors.¹²

The aim of the study is to assess the incidence of brain metastasis from different primary sites and also the effect of radiation therapy in producing relief of symptoms and in the survival of the patients with brain metastasis.

AIMS AND OBJECTIVES:

1. To study the incidence of brain metastasis from different primary sites.
2. To study the symptomatology of brain metastasis and to study the effect of radiation treatment in primary relief of symptoms.
3. To study the effect of radiation in the survival of the patients with brain metastasis.

Submission 24-01-2016, Peer Review 08-02-2016, Acceptance 15-02-2016, Published 12-03-2016.

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DOI: 10.18410/jebmh/2016/200

MATERIALS AND METHODS: This prospective study was conducted in the department of Radiotherapy, Medical College, Calicut, South India during the period 1997-1999. A total of 50 patients with brain metastasis were selected for treatment by whole brain radiation therapy.

All patients with radiological evidence of brain metastasis are included. All age groups, male and female patients are included. Postoperative patients with histopathologically proven brain metastasis referred from neurosurgery department are also included. All patients are having histopathologically proven malignancy. Biopsy was taken from primary site or from brain metastasis. All patients are interviewed personally regarding the symptoms and were examined in detail for the different system involvement.

They are subjected to whole brain irradiation. All patients are treated with Co 60 machine with a dose of 30 Gy/10F/2 weeks' period. Systemic steroids, mannitol and anticonvulsants are given during radiation treatment. During radiation treatment they were admitted and observed. After radiation treatment these patients were regularly followed up monthly. We studied the effect of radiation therapy by two parameters. One is time taken for symptomatic relief from commencement of radiotherapy. Second is the survival of each patient measured in weeks or months.

RESULTS: A total of 50 cases of brain metastasis were studied. Out of 50 cases 35(70%) were male and 38 patients (76%) were below 65 years with a median age of 54 years. There were no patients below 30 years. The most common brain metastasis was from lung cancer (n=32, 64%) followed by carcinoma breast (n=8, 16%). No primary site was detected at the time of admission in 12 cases of brain metastasis. Multiple metastasis was seen in 33(66%) and 17 patients had solitary metastasis (34%). Surgery was performed in 6 out of 17 patients with solitary metastasis. Histological evidence of adeno carcinoma was available in 21(42%) cases, squamous cell carcinoma in 20(40%), Malignant melanoma in 2(4%) and undifferentiated carcinoma in 1(2%) cases. Out of multiple symptoms patients had at presentation Headache was seen in 48(96%) cases followed by vomiting in 32(64%) case suggesting raised intracranial pressure. Neurological deficit was seen in 16(32%) and in 9(18%) cases seizures. Improvement in symptoms within one week was seen in 18(36%) cases and 37 cases (74%) had relief of symptoms before completing the course of radiation i.e., 2 weeks. During treatment 4 (8%) cases died. Median survival was 4.38 months (1-14 months) and longest survival was 14 months (n=2 cases, 4%) (Table I).

1-3 months	17(34%)
3-6 months	19(38%)
6-9 months	8(16%)
>9 months	2(4%)
Expired during treatment	4(8%)

Table 1: Survival in months

DISCUSSION: This study is aimed to assess the incidence of brain metastasis from different primary sites, its symptomatology and to evaluate the effect of radiation

therapy producing relief of symptoms and survival. This study showed maximum number of patients belonged to 5th and 6th decades (56%) of life.¹³ The median age is 54 years.¹⁴ Analysis showed 70% of male patients and 30% female.^{14,15} The predominant primary tumour in males was carcinoma lung (28 out of 35 cases=80%) and carcinoma breast (8 out of 15 cases 53.3%) in females.¹³ Out of 50 cases in this study lung (64%) and breast (16%) cancers were the commonest primary sites.² The remaining were malignant melanoma (4%),² thyroid and kidney (2% each). Brain metastasis with unknown primary is seen in 12% cases.¹⁶ The various histopathological types in this study were adenocarcinoma 42%, squamous cell carcinoma 40%, small cell carcinoma 8%, malignant melanoma 4%, large cell anaplastic carcinoma 4% and undifferentiated carcinoma 2%. As in other studies^{15,16,17,18} in our study also multiple brain metastasis are more common than solitary brain metastasis. In this study the most frequent symptom was headache.^{1,2}

Out of 50 patients studied 18 cases (36%) started showing improvement within one week and 19 patients (38%) had improvement in the second week, so total 74% (n=37) showed improvement by the end of the course of radiation treatment (i.e. 2 weeks).^{2,18} During treatment, 4 patients (8%) died due to associated visceral metastases. The observed median survival was 4.38 months, similar to other reports available median survivals ranging between 3–6 months after whole brain radiation.^{2,11} Other fractionation schedules like 40 Gy in 20 fractions, and 36 Gy in 12 fractions showed median survival rates of 6.1 months¹¹ and 4.6 months.¹⁹ respectively. It was observed that metastasis from breast cancer had good response with survival in the range of 6-14 months.²⁰ The longest survival in this series was found to be 14 months (2 cases). Both cases were adenocarcinoma with primary breast (1 case) and unknown primary (1 case). We found the median survival increased with controlled primary tumour, non-lung primary and solitary metastases.²¹ For patients with <4 number of brain metastasis, upfront SRS or surgery done before whole brain radiation treatment is more beneficial than whole brain radiotherapy alone, with a median survival of 18 months.¹⁴ Local approaches such as surgery and SRS are independent prognostic factors for survival. But the surgery is reserved for RPA class 1 patients with solitary brain metastasis.¹⁹ Upfront SRS (SRS plus WBRT) showed superior local control but survival is same as patients treated with whole brain radiation therapy (30 Gy in 10 fractions) alone.²²

CONCLUSION: Patients with brain metastasis showed lung and breast cancers as most common primary sites in male and female patients respectively. Whole brain radiation therapy with a dose of 30 Gy in 10 fractions is adequate to produce symptomatic relief in good number of patients. However long term tumour control was not achieved. Most of the studies showed that the overall survival has not improved appreciably over the past 25 to 30 years, despite advances in surgery and SRS and various combinations of the above. Hence whole brain radiation treatment continues to be the standard of care in patients with brain metastasis.

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