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## RESEARCH ARTICLE

### 8 GY SINGLE FRACTION OF RADIATION IN BRAIN METASTASIS: SINGLE INSTITUTION EXPERIENCE

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#### ABSTRACT

Brain metastasis develops in 20-40 % of diagnosed cancer patients worldwide during the course of their illness and represent most frequent neurological complications of systemic cancer as a major cause of morbidity and mortality. The cornerstones of treatment for metastatic brain disease are surgery, whole brain radiotherapy (WBRT) and radio surgery along with varying doses of steroids. As majority of patients present with multiple brain lesions which precludes the option of surgical resection and trials using various systemic chemotherapeutic agents have only demonstrated efficacy in treating brain metastases in a very selected group of primary cancers that are highly chemo sensitive. Whereas radiotherapy has been shown to be effective in treating brain metastases regardless of primary. Commonly used palliative whole brain radiation therapy treatment protocols are 30 Gy in 10 fractions and 20Gy in 05 fraction by two lateral parallel opposed fields. As most of the patients with brain metastases are with poor performance status, this retrospective study was carried out at IRNUM from 1<sup>st</sup> Jan 2016 –Dec 2016 to evaluate the efficacy of 8 Gy single fraction of radiation to whole brain in terms of relief of symptoms and median as well as overall survival. There were 21 patients .04 male and 18 females. Out of 21 included patients 14 patients were of breast cancer, 06 patients were of lung cancer and 01 patient was of gestational trophoblastic disease. All patients were diagnosed on contrast enhanced Magnetic resonance imaging (CEMRI). All patients were having multiple brain metastases. All patients were planned for whole brain radiotherapy to dose of 08 Gy single fraction by two parallel opposed lateral fields on Co-60 teletherapy machine plus steroids. Patients were monitored for relief of symptoms, median as well as overall survival.

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#### INTRODUCTION

Brain metastasis develop in 20-40% of patients diagnosed with cancer worldwide during the course of their illness and represent one of the most frequent neurological complications of systemic cancer as a major cause of morbidity and mortality (Antonadou, 2005; Gravrilovic and Posner, 2005). Overall survival for various cancers have been improved especially for breast, lung, and kidney malignancies because of advances in cancer treatment, therefore the incidence of brain metastasis have been increased (Schouten *et al.*, 2002). The aim of treatment with brain metastasis is to improve or maintain quality of life. The various treatment options are available including steroids, surgery, radiotherapy, stereotactic radiosurgery, chemotherapy (Ellis *et al.*, 2012; Goetz *et al.*, 2012; Scoccianti and Ricardi, 2011). Since majority of the patients present with multiple lesions, whole brain radiotherapy is the

standard treatment to palliate the symptoms. Median survival is one month without treatment, two months with steroids, and three to six months with cranial radiation (Ponsner, 1997; Berk, 1995). The most commonly used palliative radiation treatment protocols for brain metastases is whole brain radiotherapy (WBRT) 3000c Gy in 10 fractions or 2000cGy in 05 fractions (Mintz *et al.*, 1996; Khuntia *et al.*, 2006). The present study is a retrospective analysis of all patients who presented with multiple brain metastases, treated with WBRT of 08 Gy single fraction by two parallel opposed lateral fields on Co-60 teletherapy machine. The outcome of treatment in term of symptomatic relief, median survival and overall survival was measured and was compared with commonly used palliative treatment protocols for brain metastasis.

#### MATERIALS AND METHODS

This is a retrospective study of all patients who presented with multiple brain metastasis from Jan 2016-Dec 2016 at institute of Radiotherapy and Nuclear Medicine (IRNUM) Peshawar.

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There were 21 patients .04 male and 18 females. All patients were diagnosed on contrast enhanced Magnetic resonance imaging (CEMRI).All patients were having multiple brain metastases. All patients were planned for whole brain radiotherapy to dose of 08 Gy single fraction by two parallel opposed lateral fields on Co-60 teletherapy machine plus steroids. Patients were monitored for relief of symptoms, median as well as overall survival.

## RESULTS

Out of 21 known cancer patients, 19 patients were female and 02 patients were male. Age ranged from 24-60 years with median age of 47 years.19 patients (90%) were having multiple mets where as 02(9.5%) patients were having single metastatic lesion. Eighty-six percent metastatic lesions were found in cerebral hemisphere, twelve percent in cerebellum and two percent in brain stem. All patients presented with headache, vomiting. 08 patients (38%) presented with mental disturbance, 05 patients (23%) presented with visual disturbance, 04 (19%) presented with focal weakness, 03(14%) presented with speech difficulty as shown in Figure 1.

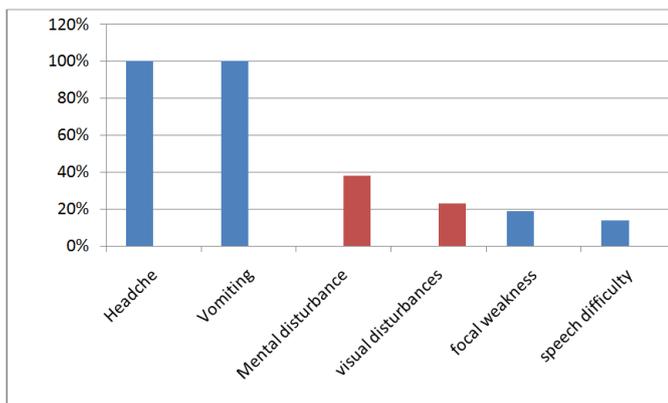


Figure 1. Signs and symptoms at time of presentation

Most of the patients were having more than one symptoms. ECOG performance status was used. Eight patients (38%) were in ECOG 1, nine patients (43%) were ECOG 2 and four patients (19%) were ECOG 3. Out of 21 included patients 14 patients were of breast cancer, 06 patients were of lung cancer and 01 patient was of gestational trophoblastic tumor (choriocarcinoma) making 67%, 28% and 5% respectively as shown in Table 1.

Table 1. Frequencies of Primary site of Malignancy

S.No	Primary Site	No	Percentage
1	Breast cancer	14	67%
2	Lung cancer	06	28%
3	Chorio carcinoma	01	05%
	Total	21	100%

Regarding breast carcinoma 09 patients (64%) were having breast cancer on the right side, 05 patients (36%) were having cancer on the left side. 11 patients (79%) were diagnosed in stage IV disease 04 with bone metastasis, 04 with brain metastasis, 02(14%) with pulmonary metastasis and 01(7%) with hepatic metastasis. 02(14%) patients were diagnosed with stage III cancer. 01 patient (7%) was diagnosed in stage II disease. 10 patients (71%) were receptor (ER/PR) negative and

04 patients (29%) were receptor positive. 02(14%) patients were diagnosed in 2<sup>nd</sup> decade of life, 03(21%) in 3<sup>rd</sup> decade, 02(14%) in 4<sup>th</sup> decade, 06 (43%) in 5<sup>th</sup> decade and 01 (7%) in 6<sup>th</sup> decade. Histopathology of all patients were invasive ductal carcinoma. Median time to develop brain metastasis was 11 months. Two patients were having controlled primary where as 12 patients were having progressive primary disease at the time of brain metastases. Six patients were diagnosed as lung cancer. 04(67%) were male and 02(33%) were female. 03(50%) patients were in 5<sup>th</sup> decade of life and 03(50%) patients were in 6<sup>th</sup> decade. 04(67%) patients presented with brain metastasis at the time of presentation. 01(16.6%) with contralateral lung metastasis and 01(16.6%) patient was treated in 2014 as stage II disease and presented with brain metastasis in 2016. Histopathology of 05(83%) patients were adenocarcinoma and 01(17%) patient was diagnosed as Squamous cell carcinoma. 01 patient of gestational trophoblastic disease (choriocarcinoma) presented with brain metastasis. Eighty nine percent of patients had improvement in most of their symptoms with complete response with respect to headache and vomiting. Overall survival for all patients was 4.4 months and median survival for all the patients was 04 months.

## DISCUSSION

Intracranial metastasis is the most common type of brain tumor in adults, with an overall incidence of approximately 8.3/100,000 (Patchell, 2003; Walker *et al.*, 1985). Brain metastasis develop in 20-40% of all cancer patients (Antonadou, 2005). Its incidence is increasing worldwide probably because of better understanding of tumor biology development of new treatment options which has led to improved survival especially for breast, lung and kidney cancers as well as advances in neuroimaging which has led to early detection of brain metastases (Schouten *et al.*, 2002). Risk of developing brain metastases varies with primary malignancy. In adults lung cancer accounts for half of all metastases (Khuntia *et al.*, 2006). Melanoma, breast, and colon cancers also carry high propensity for brain metastases. The incidence may be rising in patients with breast cancer (Tham *et al.*, 2006). In current study majority of patients with brain metastases are of breast cancer. Several factors in different series are predictive for occurrence of brain metastases in breast cancer patients like lung metastasis as the first site of relapse, negative hormone receptor status (Slimane *et al.*, 2004), HER-2 over expression, number of metastatic sites (Miller *et al.*, 2003) and younger patients with hormone receptor negative cancers (Patchell, 2003). In current study majority of patients of breast cancer were young, having stage IV disease at time of presentation with receptor negative disease relating with all factors predictive for progression of disease. The cornerstones of treatment for metastatic brain disease are surgery, whole brain radiotherapy (WBRT) and radio surgery (Schouten *et al.*, 2002; Ellis *et al.*, 2012; Goetz *et al.*, 2012). As majority of patients present with multiple lesions in brain which precludes the option of surgical resection, and trials using various systemic chemotherapeutic agents have only demonstrated efficacy in treating brain metastases in a very selected group of primary tumors that are highly chemo sensitive (Goldstein and Berkowitz, 2012; Gremmer *et al.*, 2008; Van den Bent, 2003). Whereas radiotherapy has been shown to be efficacious in treating brain metastases regardless of primary histology. (Chao *et al.*, 1954)

The ability of radiation to effectively treat brain metastases of any tumor histology is unique among currently available therapies and thus represent an important palliative option for patients with brain metastases by alleviating symptoms, decreasing the use of corticosteroids needed to control tumor associated edema (Andrews *et al.*, 2004; Bezjak *et al.*, 2001). For these reasons radiotherapy has become the cornerstone in the treatment of metastatic brain lesions. Stereotactic radiotherapy alone appears to be as effective as resection plus whole brain radiotherapy in the treatment of one or two brain metastases (Rades *et al.*, 2007). For selected patients having small lesion up to 4cm of brain metastases the addition of radio surgery boost to WBRT improves quality of life as compared to WRBT alone (Mehta *et al.*, 2005). Whole brain radiotherapy and stereotactic radio surgery therefore should be standard treatment for patients with a single unresectable brain metastasis and considered for patients with two or three brain metastases (Andrews *et al.*, 2004), but because of paucity as well as very expensive radiotherapy technique majority of the patients eligible for this radiotherapy technique cannot avail this and they have to go for WBRT as in current study. Regarding WBRT commonly used palliative radiotherapy protocol for brain metastasis is 30 Gy in 10 fractions with 3 GY per fraction. (Mintz *et al.*, 1996) Another commonly used palliative treatment protocol for brain metastases is short course of WRBT 20Gy in 05 fractions with 04 Gy each having comparable results with 30 Gy in 10 fractions. This protocol appears preferable to majority of patients having brain metastases as this is less time consuming and more convenient (Rades *et al.*, 2007). In current study all patients were planned for WBRT of 8Gy single fraction by two parallel opposed fields on Co-60 teletherapy unit, and overall and median survival was compared with other well established palliative treatment protocols (Mintz *et al.*, 1996; Rades *et al.*, 2007). The overall as well as median survival is found to comparable with other established treatment protocol. Although the sample size of this study is small but we can draw an inference that 8Gy single fraction of radiation to whole brain can be effective in relieving most of the symptoms, is cost effective ,resource sparing in busy radiotherapy institutes and feasible for patients with brain metastases.

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