ORIGINAL ARTICLE

SPECTRUM OF CAUSES OF CEREBRAL METASTASIS: A STUDY OF 16 CASES

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ABSTRACT

Background: Brain metastasis is the most common neurologic complication of systemic cancer. The aim of this study was to know about the spectrum of causes of cerebral metastasis.

Material & Methods: This cross-sectional study was conducted at Neurosurgery Department, Lady Reading Hospital, Peshawar from January 2013 to December 2014. After taking consent from ethical research committee all patients of both genders irrespective of their age who had brain metastasis based on MRI brain and histopathology results were included in the study and those with primary brain tumors confirmed on histopathology and Patients with coagulopathy, unfit for GA, not willing for surgery were excluded from the study. Patients particulars like age, gender, pre-operative symptomology, primary site of metastasis, location of metastasis and type of treatment given were recorded on predesigned proforma. Data was analyzed by SPSS version 20 and results were represented in the form of graphs and tables.

Results: We studied 16 cases; 10(62.5%) males and 6(37.5%) females. The age range was from 14 to 92 years (mean 53 years). Headache and seizures were present in 5(31.25%) cases each, weakness/hemiplegia and cognitive/behavioral disturbance in 4(25%) cases each, ataxia in one (6.25%) and one (6.25%) were asymptomatic. In 12(75%) cases Kernofsky Performance Score was >70 and in 4(25%) cases <70. Origin of cerebral metastasis was from the lungs in 7(43.75%) patients while from breast in 3(18.75%) cases.

Conclusion: Cerebral metastasis occurs in old age mostly in males. The most common mode of presentation is headache, seizures, behavioral disturbance and neurological deficits. Lung tumors have greatest propensity to metastasize to the brain.

KEY WORDS: Cerebral metastasis; Headache; Seizures; Lungs; Breast.

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INTRODUCTION

Brain metastases are the most common neurologic complications of systemic cancer in 10% to 30% of adult patients.[1] The occurrence of brain metastases reflect poor outcome and is often considered to be the terminal stage in a patient with systemic malignancy.[2,3] They are four times more common than the primary brain tumors and occur in about 25% of all patients with cancer.[4] The incidence of brain metastases is increasing because of early diagnosis due to improved imaging techniques, more frequent use of brain magnetic resonance imaging (MRI) for asymptomatic patients, and more effective systemic treatment regimens that can prolong life, permitting the cancer to disseminate to the brain.[5]

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Brain metastases are located in the brain according to the size; in the cerebral hemispheres in about 80%, in the cerebellum in 15% and in the brainstem in 5% of patients.[6] Most brain metastases originate from the lung 40-50%, breast 15-25%, melanoma 5-20%, and kidney 5-10% while in children the common sources of brain metastases are sarcomas, neuroblastomas, and germ cell tumors.[7]

Although most of these metastatic brain tumors can have a known primary site such as lung or breast carcinoma, there remain a number of cases (10-15%) in which a thorough search fails to identify the primary site.[8,9] Tumor from the primary site spreads to the brain by hematogenous root and they are located beneath the grey and white matter junction.[4] The clinical presentation of brain metastases is similar to that of other brain tumors and includes headache, focal neurologic deficit, cognitive dysfunction and seizures. Headache occurs in approximately 40% to 50% of patients with brain metastases. Focal neurologic dysfunction is the presenting symptom

in 20% to 40% of patients. Hemiparesis is the most common complaint, but the precise symptoms vary depending on the location of tumor in the brain.[10] Brain metastasis is diagnosed on neuroimaging CT and MRI brain with MRS confirmed on histopathology. Contrast enhanced computed tomography is used widely because of easy availability and low cost. Contrast enhanced MRI is more sensitive scanning in detecting brain metastases, especially small lesions or metastases situated in the posterior fossa. MRI is recommended for patients with a apparently single metastasis on a CT.[11]

Radiographically, metastases are ring enhancing lesions, located at the grey white matter junction surrounded usually by significant edema. Unlike primary brain tumors, metastatic lesions rarely involve the corpus callosum or cross the midline.[12] Along with the conventional diagnostic tools, application of the metabolic imaging modalities like SPECT, PET scan contribute further for diagnosis. Goals of the treatment are; to reduce mass effect and increased intracranial pressure; provide treatment for medical complications, such as seizures, venous thrombosis, and side effects from medication and offer definitive treatments that prolong survival and quality of life. Medical treatment in the form of steroids is the emergency treatment because it reduces brain edema.[13] Surgical resection is recommended mainly for patients with a single brain metastasis in an accessible location, especially when the tumor size is large and causing a considerable mass effect or obstructive hydrocephalus. Surgery is also recommended in patients with good performance status, who are functionally independent and in whom systemic disease is limited.

However, surgery is not recommended in radiosensitive tumors like small cell lung carcinoma, germ cell tumor, leukemias and lymphomas.[14] Surgical resection and gamma knife radio-surgery are alternative options for the treatment of patients with brain metastases.[15-18] Microsurgery, radio-surgery and radiation therapy are not given in combination, rather after surgical resection Gamma knife radiosurgery or whole brain radiotherapy is given for management of brain metastasis.[19-24] As there are many primary malignancies like lung, breast, thyroid giving rise to cerebral metastasis, but there is no local data available, so we conducted this study to know about local causes of brain metastasis, so that this grave malignancy may be timely managed.

MATERIAL AND METHODS

This cross-sectional study was conducted at Department of Neurosurgery, Lady Reading Hospital, Peshawar, Pakistan from January 2013 to December 2014. Approval was taken from the hospital ethical committee. Sixteen patients of both genders irrespective of age, admitted with the diagnosis of cerebral metastasis (diagnosed on imaging like CT or MRI brain, with MRS and other sequences confirmed on histopathology) were included in the study. Patients with gliomas or other primary brain tumors, coagulopathy, those unfit for GA and not willing for surgery were excluded from the study. Patients were admitted through OPD or casualty in case of severe seizures, headache, vomiting, or loss of consciousness. After admission all patients were subjected to detailed history, history of primary cancer and neurological examination. Hematologic tests like FBC, urea, sugar, serologic tests like HBSAg, Anti-HCV and other baseline investigations were done. All patients were operated after establishing a neuro-radiological diagnosis. Neuro-radiological investigations included CT and MRI brain with and without contrast with all sequences. Pre-operative work-up was done including fitness for general anesthesia. All patients initially managed conservatively, were put on dexamethasone and anticonvulsants. All 16 (100%) patients underwent craniotomy, biopsy and microsurgical tumor excision was done. For tissue diagnosis biopsy specimens were sent to laboratory on the same day. All cases were reported by senior pathologist. Patients were kept in ICU for 24 hours and then shifted to the ward. On 5th post-operative day all patients were discharged. Data of all patients collected. Primary cause of brain metastasis based on history, neuro-imaging and histopathology were noted. The data was collected by a performa and analyzed using SPSS version 20. Results were expressed in the form of tables/graphs/charts.

RESULTS

We studied 16 cases. Among these 10 (62.5%) were males and 6 (37.5%) females. Age ranged from 14 to 92 years (Mean 53 years). Regarding the presenting complaints, headache was present in 5 (31.25%), weakness/hemiplegia in 4 (25%), seizures in 5 (31.25%), cognitive and behavioral disturbance in 4 (25%), ataxia in one (6.25%) and one (6.25%) patients were asymptomatic. (Fig. 1)

CT or MRI brain was performed in all cases. These showed multiple lesions in 13 (81.25%) patients and single lesion in 3 (18.75%) cases. (Fig. 2) Kernofsky Performance Score was >70 in 12 (75%) cases and <70 in 4 (25%) cases. Metastatic disease was supratentorial in 13 (81.25%) and infratentorial in 3 (19.75%) cases. Surgical treatment was given to all (100%) patients.

Gross total resection was done in 3 (18.75%) and subtotal resection and biopsy was done in 13 (81.25%) patients. Primary tumors were found in 14 (87.5%) while primary site remained undiagnosed in 2 (12.5%) patients. Lung was found as the cause of cerebral metastasis in 7 (43.75%) patients, breast in 3 (18.75%), skin malignant melanoma in 2 (12.5%), genitourinary cancer in one (6.25%), gastrointes-

Table 1: Multiple variables of cerebral metastasis (n=16).

Variables of cerebral metastasis	Frequency	Relative frequency
Systemic disease	14	87.5%
No systemic disease	2	12.5%
Kernofsky Performance Score >70	12	75%
Kernofsky Performance Score <70	4	25%
Supratentorial	13	81.25%
Infratentorial	3	19.75%
Gross total resection	3	18.75%
Subtotal resection and biopsy	13	81.25%
Metastasis from lungs	7	43.75%
Metastasis from breast	3	18.75%
Metastasis from skin malignant melanoma	2	12.5%
Metastasis from genitourinary cancer	1	6.25%
Metastasis from gastrointestinal tract	1	6.25%
Metastasis from unknown primary source	2	12.5%

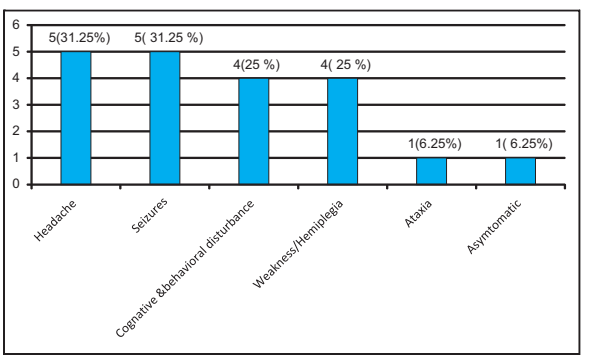

Figure 1: Pre-operative signs and symptoms of patients with cerebral metastasis (n=16).

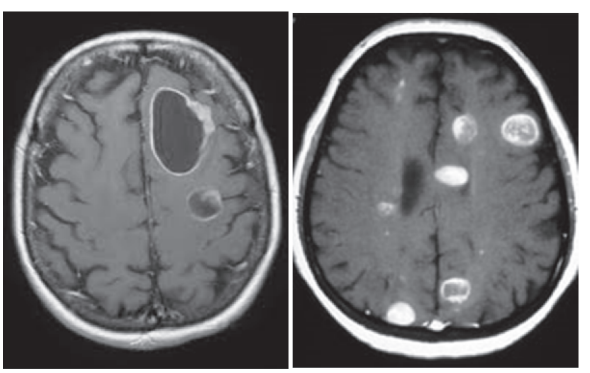

Figure 2: MRI of brain showing cerebral metastases.

tinal tract in one (6.25%) and primary source was undiagnosed in 2 (12.5%) patients. Whole brain radiotherapy was given to 2 (12.5%) patients before surgery. (Table 1)

DISCUSSION

We studied 16 cases of brain metastasis and evaluated them for the causes. In the last 50 years, there has been nearly a five-fold increase in the overall prevalence of brain metastases and the ratio between metastatic to primary brain tumors is now almost equal. Brain metastases significantly increase the morbidity and mortality in cancer patients.[25,26] Tumors from distant areas spread to the brain through a vicious circle: tumor from the primary organ (e.g. breast cancer) transformation, genetic change, growth angiogenesis, invasion, transportation, intravasation into blood or lymph vessel, circulation, arrest in 1st capillary bed of CNS organ (brain, leptomeninges), transportation inside brain, passage to arterial circulation, arrest in CNS capillary bed, extravasations, angiogenesis and growth.[27-33]

Patients with brain metastasis commonly present with headache, seizures, hemiplegia, cognitive and behavioral abnormalities. In our study we found headache in 31.25% patients, seizures in 31.25% hemiplegia in 25% and cognitive and behavioral abnormality in 25% patients each. In a series headache was reported as the commonest clinical presentation observed in 49% of patients followed by mental changes in 32%, focal weakness in 30% and seizures in 18% of patients which is comparable to our study regarding headache, but they found focal weakness as second more frequent symptom. Victor[35] found that headache in 42% and seizure in 21% as the two most common presenting symptoms. In addition, 35% of patients had cognitive dysfunction and 30% had motor dysfunction. His results are comparable to our study.

Inside the brain cerebral metastasis are more common in supratentorial as compared to infratentorial compartment. In our study we had supratentorial lesions in 81.25% patients and infratentorial in 19.75% patients. Approximately 80% of lesions were found in the cerebrum, 15% in the cerebellum and 5% in the brainstem as opined by Nussbaum et al.[36] Our results are closer to their results.

We evaluated all patients for primary source causing cerebral metastasis. Lung was the cause of cerebral metastasis in 43.75% cases, breast in 18.75%, skin malignant melanoma in 12.5%, genitourinary and gastrointestinal cancer in 6.25% patients each, while the primary source was unknown in 2 12.5% patients. Victor studied 2700 cases in New York Cancer Center and showed the distribution of primary cancers as 48% lung, 15% breast, 9% melanoma, 1% lymphoma, 3% gastrointestinal, 11%

genitourinary (21% kidney, 46% testes, 5% cervix, 5% ovary), 10% osteosarcoma, 5% neuroblastomas and 6% head and neck tumor.[35] Our results closely correlate with his results. While Lassman and De Angelis reported percentages of patients developing brain metastases for specific primary histologies as 18 64% lung cancer, 2 21% breast cancer, 2 12% colorectal cancer, 4 16% melanoma, 1 8% kidney, 1 10% thyroid and 1 18% unknown primary.[37] In that study colorectal cancer was the 3rd common cause of cerebral metastasis, while in our study we had malignant melanoma the 3rd common cause of cerebral metastasis. Limitation of our study was that we had small number of patients.

CONCLUSION

Cerebral metastasis occurs in old age people mostly in males. The most common mode of presentation is headache, seizures, behavioral disturbance and neurological deficits. Lungs tumors have greatest propensity to metastasize to the brain.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.