

Research

Descriptive Analysis of Cerebral Metastasis in a Tertiary Care Centre; the Indian Perspective

Pradeep Kumar Gunasekaran¹, Krishna Narayanan^{1*}, R. Lakshmi Narasimhan¹, Arumugam Thiruvalluvan¹

¹Rajiv Gandhi Government General Hospital and Madras Medical College, Chennai, Tamil Nadu, India

Abstract**Introduction**

The Incidence of Cerebral metastases is increasing the world over, owing to factors such as gradual aging of the population, improved treatment of primary malignancies and the availability of sophisticated imaging. To date, studies arising from the Indian scenario are lacking and Physicians in India tend to rely on, often antiquated, data from other countries. This study aims to bridge that gap.

Methods

This was a prospective study conducted in Madras Medical College, Chennai. 255 patients documented to have Intracranial Metastases by PET/CT imaging were enrolled into the study. Tumours were divided by their location and number (mono-centric or multi-centric). This was correlated with the gender of the patient and the location of the primary lesion (if known) to allow for characterisation.

Results

A larger number of patients had multicentric metastases and there was a definite female preponderance. Monocentric metastasis was more commonly found in the Frontal region while multicentric metastases were more commonly found in the posterior fossa. Overall the most common primary was found in the lung, with the lung being the most common in men and the breast in women.

Conclusion

Many differences were found between available literature and the patients in this study, in terms of the location of the primary and the distribution of the metastases. This likely reflects the heterogeneity of malignancies in India as well as the pattern of metastases.

Introduction

Cerebral metastasis as a disease entity is gradually increasing in

incidence the world over, however the exact incidence remains largely unknown [1]. Most studies describing the patterns of cerebral metastasis have been conducted in other countries and Indian studies have mostly been restricted to pathological evaluations in a retrospective fashion [2]. This lack of data has significant implications as the outcome for patients with cerebral metastasis has evolved over the years. Once considered a disease with a uniformly unfavourable prognosis [3], the spectrum of treatment modalities available in the modern era allows for treatment strategies that can offer meaningful improvements in terms of morbidity and mortality. An understanding of the source of metastasis, location of the metastasis, number of metastases and the distribution of these metastases has implications in both patient care and planning for the challenges of caring for this population of patients as well as developing preventative measures to decrease the likelihood of metastatic brain disease.

Subjects and Methods

This was a prospective study conducted at the Institute of Neurology/Neurosurgery, Rajiv Gandhi Government General Hospital and Madras Medical College. The study was conducted after obtaining clearance from the Institutional Ethics Committee and after obtaining consent from subjects involved in the study.

***Corresponding Author:** Krishna Narayanan, Resident in Neurosurgery, Madras Medical College, Park Town, Chennai, Tamil Nadu, India, E-mail: mdknarayanan@gmail.com

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Methods

255 patients documented to have cerebral metastasis as diagnosed by Positron emission tomography/ Computed Tomography (PET/CT) were enrolled into the study. The radiological profile of each patient was analysed, and characteristics of the lesion(s) were sequentially tabulated. Tumours were divided by their location and number (mono-centric or multi-centric). This was correlated with the gender of the patient and the location of the primary lesion (if known) to allow for characterisation.

Results

A total of 255 patients were studied using PET/CT data. The results

were tabulated using Excel sheets and statistical analysis was carried out using the IBM SPSS software for windows.

Mono centric vs Multi centric metastasis

75 patients (of 255) were found to have monocentric metastasis. In these patients the most common location was the Frontal region (23 patients / 30%). The second most common region was the Parietal region (19 patients /25%). 17 patients (22%) had metastasis in the cerebellum. Rarer sites of metastasis included the Corona Radiata (1 patient) and the Supra sellar region (1patient).

	Right			Left			Bilateral			Total		Total
	M	F	T	M	F	T	M	F	T	M	F	
Frontal	3	7	10	5	6	11	-	2	2	8	15	23
Parietal	3	6	9	4	4	8	-	2	2	7	12	19
Occipital	2	2	4	1	2	3	-	-	-	3	4	7
Temporal	-	-	-	1	2	3	-	-	-	1	2	3
Corona Radiata	1	-	1	-	-	-	-	-	-	1	-	1
Corpus Callosum	-	-	-	-	-	-	-	2	2	-	2	2
Suprasellar	-	-	-	-	-	-	-	1	1	-	1	1
Ganglio - Capsular	-	-	-	-	2	2	-	-	-	-	2	2
Cerebellum	3	4	7	1	4	5	-	1	1	-	-	17
Vermis							2	2	4	6	11	
Total	12	19	31	12	20	32	2	10	12	26	49	75

Table 1: Mono- Centric Metastasis: Location wise distribution of Mono centric metastasis, with a total of 75 patients. 26 male and 49 Female 180 patients (of 255) were found to have multicentric metastasis. These patients showed a higher preponderance for involvement of the cerebellum (52 patients /29.4%) which was followed by the Frontal region (33 patients / 18%) and the Parietal region (27 patients / 15%). Rare sites included the Suprasellar region (1 patient) and the Ganglio – capsular region (1patient).

	Right			Left			Bilateral			Total		Total
	M	F	T	M	F	T	M	F	T	M	F	
Frontal	5	10	15	1	8	9	6	3	9	12	21	33
Fronto - Parietal	-	1	1	1	2	3	1	3	4	2	6	8
Parietal	3	5	8	4	6	10	4	5	9	11	16	27
Parieto - Occipital	4	-	4	-	3	3	-	-	-	4	3	7
Occipital	3	1	4	2	2	4	1	1	2	6	4	10
Temporal	3	5	8	4	5	9	1	3	4	8	13	21
Centrum Semiovale	1	1	2	-	1	1	-	-	-	1	2	3
Suprasellar	-	-	-	-	-	-	-	1	1	-	1	1
Thalamus	1	1	2	1	1	2	-	-	-	2	2	4
Thalamo - Capsular	-	1	1	2	-	2	-	-	-	2	1	3
Basal Ganglia	-	1	1	-	-	-	-	1	1	-	2	2
Ganglio - Capsular	-	1	1	-	-	-	-	-	-	-	1	1
Cerebellum	6	10	16	4	4	8	9	18	27			
Vermis							-	2	2	19	34	53
Midbrain	-	-	-	-	-	-	-	1	1	-	1	1
Pons	1	-	1	1	2	3	-	1	1	2	3	5
Medulla	-	-	-	-	-	-	-	1	1	-	1	1
Total	27	37	64	20	34	54	22	40	62	69	111	180

Table 2: Multi- Centric Metastasis: Location wise distribution of Multi centric metastasis, with a total of 180 patients. 69 male and 111 Female Gender distribution of the total patients studied 95 patients were male and 160 were female. The location of the tumours in terms of both monocentric and multi centric metastases was comparable among both sexes.

Characteristics of the Primary Lesion

When both the sexes were considered in to, the most common primary was the lung (86 patients / 33%). When the sexes were considered separately, the most common primary site in males was the lung (55 patients / 57%) and in females was the breast (79

patients / 43 %). Other primary sites included the Cervix (14patients), Endometrium (8 patients) and Ovary (11patients) in females and the Colon,Cricopharynx,Esophagus, Bladder, Kidneys, Tongue and metastases from malignant melanoma in both sexes. 4 males were found to have a primary lesion in the prostate. The remainder of the patients had an unknown primary lesion (10patients).

	Male	Female	Total
Bladder Ca	5	1	6
Breast Ca	1	79	80
Cervix Ca	-	14	14
Colon Ca	6	8	14
Cricopharynx Ca	1	-	1
Endometrial Ca	-	8	8
Esophagus Ca	6	2	8
Lung Ca	55	31	86
Melanoma	4	3	7
Ovary Ca	-	11	11
Prostrate Ca	7	-	7

Renal Ca	2	-	2
Tongue Ca	-	1	1
Unknown Primary	8	2	10
Total	95	160	255

Table 3: location of Primary tumour in patients diagnosed with cerebral metastases (mono / multi centric)

Discussion

There has been a significant paradigm shift in the approach and management of cerebral metastasis. Once considered a fatal disease, advances in micro neurosurgery and intensive care have paved the way for treatment modalities that include microsurgical excision [4], Whole Brain Radiotherapy (WBRT) [5] or Stereotactic Radio surgery (SRS) [6]. The management of any disease begins with a thorough understanding of the disease process and quantifying the Incidence of the disease and formulating a ‘Problem Statement’. While there is no uniform consensus on the exact incidence of cerebral metastases, the fact that this disease entity is growing the world over is evident. Factors responsible for this may include, better treatment of primary malignancies, increased Overall Survival (OS) in patients harbouring cancer and an increase in cancer as a disease due to the gradual aging of the population. Indian Neurologists and Neurosurgeons are currently reliant on data regarding cerebral metastases obtained from studies conducted in the United States [7], Scotland [8] and other populations such as Iceland. Moreover, the data obtained from these studies significantly under estimate the disease burden as most predate the use of sophisticated imaging technology and therefore likely under estimate the true incidence and prevalence of metastases to the brain [9]. The data extrapolated from these studies are, unfortunately, non-representative of the Indian population, that finds itself juxtaposed between the developed and developing world. The only available data for the Indian population stems from a single article that took into consideration pathological samples obtained from biopsies and surgical specimens [2], this data is again from a small portion of the population that underwent surgical excision and/or surgical biopsy, thereby leaving out a number of patients who were not candidates for surgical intervention or declined surgical intervention. This introduces a significant bias into the above-mentioned study. This study aims to bridge that gap and provide data in the Indian scenario. Upon analysing the data from PET images, tumours were defined as mono-centric, i.e. a solitary metastasis, or multi centric, i.e. multiple metastases. Established literature dictates that most metastases occur in the distribution of the Middle Cerebral Artery (MCA) [10], while this pattern was evident in mono-centric metastasis, Multi centric metastases showed a predilection for the posterior fossa, specifically the cerebellum. While Cerebellar metastases are considered rare in most reported literature [10], our population data showed a significant number of cases with tumours in this location. Rarer sites of metastases included the Suprasellar and Gangliocapsular region

in Multicentric metastases and the Corona radiata in monocentric metastasis, these sites prove to be challenging while considering surgical excision and therefore must be treated with other modalities such as SRS and WBRT. The sample that we studied showed a female preponderance, likely representing the referral pattern of the Institute at which the study was conducted. The location of the metastasis (es) was comparable among the sexes, indicating that gender does not play a significant role in the seeding of tumours. The characteristics of the primary offending lesion revealed that, as in most published literature [9], the most common source of secondaries in the Indian population, across both genders, was the lung. While accounting for the difference in genders, for males the most common location was from the lung and for women it was from the breast. This again is in accordance with internationally available literature [11], likely representing the changing demographics of the Indian population. Of importance here were metastases from gynaecological malignancies such as the Cervix, Endometrium and the Ovary, these malignancies rarely metastasise to the brain, however due to the sheer incidence of such tumours in India, a significant number of such tumours do present themselves to the treating physician. Gender does not play a significant role in the incidence of cerebral metastasis except in the case of malignant melanomas which shows a male preponderance [12]. The fact that melanoma primaries in men develop in locations that are more likely to spread to the brain, namely the head, neck, and trunk, could be a potential explanation for this observation [13]. Such an observation could not be established in this study due to the relatively low accrual of patients with Malignant Melanoma, likely due to its lower incidence in the Indian population. Other sites of primary lesions included the colon, the cricopharynx, the esophagus and the bladder. Lastly a significant number of patients presented with metastases of an Unknown primary (10patients) that remained unknown despite radio nucleotide imaging and biopsy. This again is in concordance to available literature, wherein studies have found an incidence of metastasis from an unknown primary to occur in 5% of cases [14]. This study taken up on a cross section of the Indian population harbouring primary tumours in various location provides us with a glimpse into the metastatic pattern in the Indian subcontinent. Significant among this is a preponderance for Cerebellar metastases and metastases from lesions within the ovary, cervix and endometrium. This information is of vital importance as it allows for enhanced screening programs in this population as well as aiding in the diagnosis and management of such entities. Moreover, this data should benefit policy making and systemic changes in a country that has failed to create a centralised

database on a war footing. Studies such as this focussing on a given population are therefore essential to tailor treatment strategies as it is imprudent to generalise fundamentally different populations.

Conclusion

Cerebral metastases have evolved from a disease of palliation to a disease where aggressive treatment can provide meaningful survival and cure in a select group of patients. While it is universally recognised that the incidence of this disease entity is on the rise, adequate population data and disease burden data is unavailable in India. This study aims to be a step in the direction of establishing such data that will therefore allow treating physicians to better formulate screening protocols, treatment strategies and allow for policy change to address the magnitude of the problem.

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