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Original Article

Stereotactic Radiosurgery in Brain Metastases at a Tertiary Cancer Center in Kashmir: A Novel Experience

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Abstract

Background and Objective: With improvised cancer care the incidence of brain metastases is increasing worldwide. Traditionally whole brain radiotherapy, corticosteroids, and surgery have been the mainstay of treatment. Stereotactic radiosurgery (SRS) has evolved as a promising modality in the management of brain metastases, either alone or in combination with other modalities. We share our experience of SRS in brain metastases at a tertiary cancer center in Kashmir, India.

Materials and Methods: One hundred and twenty patients with radiologically or histologically documented brain metastases were addressed for their demographic profile of which 37 were analyzed with respect to their clinico-dosimetric profile.

Results: Thirty-seven patients received SRS, predominantly hypofractionated schedule. The majority were males with underlying lung cancer.

Conclusion: The present analysis, besides highlighting the increasing trend of incidence of brain metastasis also suggests the feasibility of linear accelerator (LINAC)-based SRS in brain metastases owing to the wide availability of LINAC-based radiotherapy machines, ease of execution, and non-operative alternative.

Key words: Brain metastases, Kashmir, Stereotactic radiosurgery, Whole brain RT

INTRODUCTION

Brain metastases are one of the most frequent neurological complications of cancer.[1] For the majority of brain metastases, lung cancer is the most common primary site and over 25% of cancer patients develop brain metastases at some point in their disease course.[2]

The management of brain metastases has undergone a paradigm change over the last one and a half decades with respect to techniques of radiotherapy as well as novel chemotherapeutic and immunotherapeutic drugs.[3]

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Whole brain radiotherapy (WBRT) has traditionally been used, for multiple brain metastases; however, cognitive impairment associated with WBRT has been a significant clinical problem and concerns with WBRT-associated neurocognitive toxicity have contributed to greater use of SRS for patients with solitary and even multiple metastases.[3]

SRS has evolved as a promising method of delivering high-dose radiation using a linear accelerator (LINAC) or multiple cobalt-60 sources (Gamma Knife) to the target lesion. Multiple focused radiation beams intersect over a target, resulting in the delivery of a highly conformal, high-dose of radiation to the target and minimal radiation to surrounding normal tissues with preservation of neurocognitive functions.[4]

MATERIALS AND METHODS

This analysis was conducted in the Department of Radiation Oncology, Government Medical College, Srinagar, over a

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Table 1: Clinical profile

S. No.		Demographic variable		Number		Percentage
1	Age	<40= 39	33	<40=39		33
				>40= 81	67	67
2	Gender	M=78	65	M=78		65
				F=42	35	35
3	Family history of cancer	Y=05	04	Y=05		04
				N=115	96	96
4	Diet	V= 00	0	V=00		0
				NV= 120	100	100
5	Tobacco	Y=75	63	Y=75		63
				N=45	37	37
6	H/o Any previous Radiation exposure (other than for primary cancer)	Y=0	0	Y=0		0
				N=120	100	100

period of 02 years. It was a retrospective analysis conducted on 37 patients who had radiological or histological documentation of brain metastases. All patients were treated with LINAC-based SRS (TrueBeam). Patients were assessed with respect to their clinico-demographic profile and dosimetric correlates of stereotactic radiotherapy to brain metastasis.

RESULTS

There were 120 patients with brain metastases from 2021 to 2023. These included those who had presented with brain metastasis, developed during treatment (synchronous metastases, 23%), or whereas on follow-up (77%). The majority of the patients were males (65%) and were more than 40 years of age (67%). Most of the patients (63%) had a history of tobacco use whereas 05 had a family history of cancer [Table 1]. There was no history of radiotherapy in the past other than for the primary cancer for which patients were being treated. Of these 120 patients, 37 (31%) were taken for SRS. Forty-five metastatic brain lesions were irradiated in these 37 patients using stereotactic radiotherapy. The majority of the patients subjected to SRS had oligo-metastatic (<04) brain metastases. Thirty-one of these patients had solitary metastasis, one had four metastases whereas five patients had two metastases. Of all the metastases, 86 patients had supratentorial metastasis, 24 had both supra and infratentorial whereas 10 had only infratentorial metastasis. The majority of the patients presented with headache and nausea/vomiting (>85%). Lung and breast were the most common primaries combined (67%), Table 2 and adenocarcinoma was the predominant histology (60%). The median volume of metastatic lesions was 5.5 cm^3 and the mean size of metastatic lesions was 2.5 cm. Most of the metastatic brain lesions were in the range of 2–3 cm. Disease progression at the primary site was seen in 15 patients, 17 had partial response whereas three had primary in remission. Nearly half of the patients had received all the modalities of treatment (surgery, chemotherapy/immunotherapy, and radiation for the primary). Seventeen patients (46%) had received single fraction SRS whereas the rest had received hypofractionated SRS (HF-SRS). Twenty Grays (20Gy) was the median dose of SRS that was delivered. Of the 37 patients, 32 were treated mono isocentrically. The non-coplanar technique was used in the majority of the patients (78%). Thirty patients were treated naïve and seven patients were re-irradiated. Of the treatment naïve patients, two had undergone metastasectomy and received post-operative SRS. Of the re-irradiated patients, four had received WBRT earlier and three had received SRS. "Planning target volume (PTV) dose fall off" to 50% of the prescribed dose was limited to 0.8 mm and the mean conformity index (CI) was around 0.9 Table 2.

DISCUSSION

Brain metastases are a frequently encountered sequel of cancer accounting for nearly 10–15% of all cancers. The prognosis is typically grim with patients surviving only a few months after diagnosis of brain metastases. Traditionally, corticosteroids have been the mainstay of treatment followed by WBRT which has prolonged survival only by a few months.[5]

Over the years clinical trials have shown WBRT to be associated with neurocognitive impairment and that nearly half of the patients die of intracranial progression of the disease.[6] Finally, it has been realized that preserving neurocognitive functions is as important as prolonging survival.[7] Whereas surgery could be a viable option for a solitary brain metastasis with significant mass effect, warranting an immediate decompression, it is not a modality of choice in patients with multiple metastases and low-performance scores.[8]

SRS has evolved as an effective alternative approach besides surgery or hippocampal avoidance WBRT in which lesions close to hippocampi cannot be considered for HAWBRT.[9]

Table 2: Clinical profile

S. No.	Variables	Number	Percentage
1	Primary	Lung=52	44
		Breast=44	37
		GIT=10	08
		GU=04	04
		Gynecological=03	02
		Skin and others=07	05
	Histology	Adenocarcinoma=72	60
		Squamous carcinoma=21	18
		Small cell=27	22
2	Brain secondaries	Synchronous=28	23
		Metachronus=92	77
3	Status of primary malignancy	Not treated=10	08
		Complete remission=10	08
		Partial response=36	30
		Progression=64	54
4	Type of treatment to primary	Surgery=04	03
		Chemo/radiotherapy T=43	36
		Surgery/ chemoradiotherapy=53	44
		Surgery/chemoradiotherapy immunotherapy=20	17
5	Signs and symptoms of metastasis (includes more than one parameter also)	Headache=80	66
		Nausea and vomiting=76	63
		LOC/alt sensorium=22	18
		Paresis=13	10
		Seizures=12	10
6	MRI location of metastasis	Supratentorial=86	72
		Infratentorial=10	08
		Supra- and infra-tentorial=24	20
7	Distribution of metastases in patients	Solitary=31	72
		Multiple=06	28
8	Size of metastasis for SRS	Up to 2 cm=12	28
		2–3 cm=30	65
		>3 cm=03	07
9	Volume of metastases for SRS	5 cc=20	44
		5–10 cc=17	38
		>10 cc=08	18
10	Mono-isocentric	32	86
	Multi-isocentric	05	14
	Non-coplanar	29	78
	Coplanar	08	22
11	Only SRS	28	75
12	SRS after WBRT	04	11
13	SRS after metastasectomy	02	05
14	RE SRS	03	09
15	Single fraction SRS	17	46
16	Hypofractionated SRS (FSRT)	20	54
17	Dose prescribed (80% isodose)	18 Gy=09	24
		18–20 Gy=20	54
		>20 Gy=08	22
18	Conformity index	01=03	07
		0.8–0.9=38	84
		01–1.2=04	09

Stereotactic radiosurgery was pioneered in the early 20th century by Swedish neurosurgeon Lars Leksell. It involves the delivery of multiple radiation beams which intersect at a target with a pinpoint precision. A single high dose of radiation is delivered with a very rapid dose fall-off to minimize the risk of damage to any adjacent normal tissue. Gamma Knife was the first commercial intracranial SRS system that was used for brain metastasis. It involved using multiple fixed cobalt sources, beams of which were directed precisely to the target with surgical immobilization of the skull to manage motion.[10] Radiobiology of high-dose SRS is different from fractionated radiation therapy. Fractionated radiation primarily mediates tumor kill from DNA double-strand breaks by reactive oxygen species while as in high dose SRS, vascular damage and tumor antigen release play an important role. The ablative nature of SRS may also increase antitumor immune response given increased antigen release.[11]

Over the years many modifications and improvisations in the execution of stereotactic radiation delivery have led to the use of LINAC-based stereotaxy. Stereotactic radiosurgery is now available worldwide, and it is increasingly being used to treat brain metastases because it is less invasive compared to surgical intervention, and can be offered to patients with low-performance scores, multiple brain metastases, and patients with pre-existent neurocognitive dysfunction.[12]

SRS can be delivered as a single high-dose radiotherapy (single fraction SRS) or in a fractionated form of 03 to 05 fractions called HF-SRS.[13] In our analysis, nearly half of the patients (46%) received single fraction SRS whereas the rest received HF-SRS [Table 2]. The decision of fractionation was predominantly dictated by the dosimetric constraints of nearby organs at risk (OAR), size (volume) of the metastatic lesions, patient symptomatology, and to a lesser degree by patient PS. Lesions close to eloquent brain structures such as optic chiasm and brain stem and size >4 cm were preferably treated with fractionated SRS. Single fraction SRS is traditionally used for lesions <4 cm. As per the recommendations of the radiation oncology working group, 90–05 doses per fraction of SRS have varied from 24 Gy, 20 Gy, and 15 Gy for sizes <2 cm, 2 cm, and >2 cm, respectively, in most series.[14] In our study, 45 metastatic brain lesions were irradiated. All patients except one had oligo-metastatic (<04) brain metastases. There were 31 patients who had solitary (single) metastasis, one patient had four metastases and five patients had two metastases each. Over 70% of patients had metastatic lesions around 2–3 cm. Historically no association has been found between the location of the metastatic lesion (supra- or infra-tentorial) as regards to the site of primary malignancy. The majority (84%) of patients had supratentorial metastases in our analysis as corroborated by other literature.[15]

SRS has been used across various clinical scenarios in metastatic brain disease. Current uses for stereotactic radiosurgery include delivery as a boost after whole-brain

radiation therapy; sole modality for patients with a limited number of brain metastases; in pre- or post-operative settings; and combination with systemic, targeted, and immune-based therapies;[4] however, prospective, randomized data on stereotactic radiosurgery versus any of the other modalities, and its use in combination with systemic therapies are limited.[4]

In our analysis, 30 patients were treated naïve and seven patients were re-irradiated. Of the treatment naïve patients, two had undergone metastasectomy and received post-operative SRS. Of the re-irradiated patients, four had received WBRT earlier and three had received SRS.

With encouraging results from stereotactic radiotherapy in brain metastasis, the emphasis nowadays is to improvise on dosimetric parameters to enhance local control. A CI is one of the indices as to how well the volume of a radiosurgical dose distribution conforms to the size and shape of a target volume.[16] Because the success of radiosurgery is related to the extremely conformal irradiation of the target, an accurate method for describing this parameter is important. The ICRU report 62 defines CI as, CI = TV/PTV where TV is the treated or target volume enclosed by a given isodose surface (e.g., 100% and 50%) and PTV is the planning target volume. By convention, a perfect conformity score is a unity, whereas a deviation from perfect conformity gives a higher or lower score. With the PITV ratio, a value > 1 suggests overtreatment (spillage of isodose outside target PTV) in most cases, whereas a value < 1 suggests undertreatment.[17] Our patients had a mean CI of 0.9.

CONCLUSION

With increasing life expectancy, the number of cancer patients with brain metastases is increasing. WBRT and metastasectomy have demerits of cognitive impairment and being an "invasive procedure," respectively. SRS appears to be a promising method of addressing brain metastases, though large randomized studies are warranted to justify its superiority in all clinical aspects.

SRS is a novel experience in Kashmir Valley. Lung cancer happens to be the most common "primary" and "indication" for brain metastases and execution of SRS, respectively, in our setup. Headache was the most common presenting symptom. Males over 40 were commonly affected and predominantly HF-SRS schedule was used keeping in view the dose constraints of OARs.

AUTHORS DECLARATION

We have not addressed the clinical outcome of these patients as the patient cohort was less and follow-up time was not optimum to deliberate on toxicity and survival statistics.

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