Kasr. El-Ain. J. of Clin. Oncol. Nucl. Med.
Vol.2, no.2, Apr. 2006:37-41

NEMROCK

Original Article

LINAC RADIOSURGERY TREATMENT RESULTS OF BENIGN MENINGIOMAS

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ABSTRACT

Background: Stereotactic radiosurgery has emerged as an established treatment modality of intracranial tumors. It is used as an alternative to surgery or to supplement subtotal surgical resection of locally invasive tumors.
Aim of the Work: To demonstrate the efficacy and safety of stereotactic radiosurgery in treatment of benign meningiomas.
Patients and Methods: twenty-six patients with 28 benign meningiomas were prospectively treated with 6-MV modified linac (Photon Knife) in a non-randomize clinical study. Mean age was 54 years (± 10.5, range: 25 to 75 years). Dose was given in single or multiple fractions depending on tumor location. Winston-Lutz test for accuracy of isocentre localization was performed in all cases. Regular clinical and radiological follow up was carried out.
Results: The mean tumor volume was 16.3 cc (± 9.64, range: 1.85–32.56cc). Mean tumor edge dose was 17 Gy (± 2.9, range: (13 to 24Gy). All patients tolerated the treatment well. The follow up period ranged between 11 months and 42 months (mean: 28 ± 8.15 months). Clinical improvement occurred in 10.5%, deterioration occurred in 10.5%, whereas 79% remained stable. Radiological tumor control was achieved in 89.5%, while 10.5% of tumors continued to grow.
Conclusion: Stereotactic radiosurgery provided high rates of tumor growth control, often with tumor regression, and low morbidity rates in patients with benign intracranial meningiomas. It is a useful treatment modality which can supplement subtotal surgical resection of sizable benign meningiomas or can be used as an alternative to surgery for recurrent tumors, for patients who have severe systemic illness or those who refuse to have open surgery.

Key Words: Meningiomas, linac, radiosurgery, treatment results

INTRODUCTION

Meningiomas constitute about 15% to 20% of all brain tumors and are the most common benign intracranial tumor. They are usually diagnosed in middle age, and are significantly more frequent in females than in males. Majority of them are benign tumors, some are locally invasive into nearby critical structure precluding its total removal[1, 2].

The treatment of choice for intracranial meningiomas is complete surgical excision. However, meningiomas may recur, even after apparent gross total removal. In addition, curative resection can be a morbid undertaking because of tumor location, involvement of critical structure, advanced patient age and/or comorbid conditions[3,4].

Skull base tumors are relatively inaccessible tumors with complex neuro-vascular anatomy. Despite technical advances and growing experience in the past two decades, microsurgery of skull base tumors is still associated with significant postoperative complications and high recurrence rate[3,4].

Parasagittal meningiomas, especially when associated with the middle or posterior third of the superior sagittal sinus, pose difficult management challenges. Initial surgical excision is associated with high morbidity and frequent tumor recurrence after subtotal resection. Neurological deficits are cumulative when multiple resections are required. No consistent management approach exists for patients with such tumors[5]. Despite advances in microsurgery, tentorial meningiomas continue to challenge surgeons and patients[6].

Conventional radiotherapy provides an alternative to surgery in patients with medical contraindication to surgery, inaccessible tumors, subtotal resection, old age, recurrent tumors and patients refusing surgery. It provides longer periods of progression free survival attainable with law morbidity. However, the role of conventional radiotherapy is also limited by the presence of radiosensitive normal structures close to these tumors[7,8].

Stereotactic radiotherapy (SRS) is a single fraction technique that uses stereotactic principles for targeting and treatment of intracranial lesions through the use of multiple non-coplanar beams[9]. It has emerged as an alternative to microsurgery to supplement subtotal surgical resection of locally invasive tumors and/or recurrence after surgical treatment[6, 10, 11].

The aim of this study is to present the treatment results of 26 intracranial benign meningioma patients using Linac SRS to demonstrate the safety and efficacy of SRS in treatment of these tumors.

PATIENTS AND METHODS

twenty-six patients with 28 intracranial benign meningiomas were selected for treatment at Al-Hekmah and El-Khair International Hospitals, Mansoura, Egypt with 6-MV modified linac (Photon Knife) in a non-randomize clinical study during the period March 1998 to March 2000. Selection criteria for these patients included patients with residual tumors after surgical resection, recurrent tumors, old age <65 years, unstable medical problems, and multiple lesions. Exclusion criteria included large tumors (tumor diameter <40mm, volume 33cc.), marked neural compression, high intracranial pressure and hydrocephalus, and Karnofsky Performance Scale 60 or less. Before treatment, patients were assessed by clinical examination, CT and/or MRI, and tissue diagnosis in patients who had previous surgical resection. The treatment procedures were explained to each patient before starting treatment with the possible treatment outcome and side effects. Written consent was signed by the patient before stating treatment.

Stereotactic head frame fixation was applied to the patient under local anesthesia followed by high-resolution contrast-enhanced CT imaging. Stereotactic head mask system was applied for patients who would have more than one fraction. Data transfer to planning computer, target volume determination and localization and 3-Dimesional (3-D) planning were carried out in El-Hikmah Hospital (using software of BrainScan v3.5, BrainLAB GmbH, Germany).

Treatment planning was always performed by a neurosurgeon, radiation oncologist, and radiation physicist. The dose selection for each patient was influenced by tumor volume, tumor location, presence of radiosensitive structure nearby, previous history of radiation therapy and patient's age. Dose planning was performed to keep optic nerve and chiasma dose below 9Gy. Treatment verification and delivery were carried out in El-Khair International Hospital using modified 6MV linear accelerator. Quality assurance measurements were carried out according to the recommendations of American Association of Physicists in Medicine (AAPM report No. 54)[12]. Verification of mechanical parameters of the system is carried out before each treatment by checking gantry and table alignment using optical beam, and alignment of the isocentre with the wall mounted laser beams. Winston-Lutz test for accuracy of isocentre localization is carried out for each patient before each treatment[13].

Patients were discharged within 24 hours after radiosurgery. Post treatment, patients were clinically assessed every month, and radiologically by CT and/or MRI every three months. Clinical criteria for assessment of treatment response included: Clinical response if there is more than 50% decrease of patient's symptoms and signs, stable disease if there is less than 50% decrease of patient's symptoms and signs, and no response if there is progression of patient's symptoms and signs or appearance of new symptom(s) and sign(s) related to the disease. Criteria for radiological tumor control are defined as decreased or no change of tumor size, and/or loss of tumor enhancement on CT or MRI. Statistical Analysis: Statistical analysis was done using SPSS (Statistical Package for Social Science) program 10th version, 1999. Mean (±SD) and percentile ratio are used to describe our data (simple descriptive statistics).

RESULTS

Of 26 patients with 28 intracranial benign meningiomas included in this study, there were 10 males and 16 females with mean age of 54 years (± 10.5, range: 25 to 75 years). They included 14 patients (54%) with residual tumors after surgical resection, recurrent tumors in three patients (11.5%), old age <65 years in three patients (11.5%), unstable medical problems in 4 patients (15%), and multiple lesions in two patients (8%). Tumors were located at skull base in 19 patients (73%), falcine/parasagital in four patients (15%), tentorial in 2 patients (8%), and convexity meningioma in one patient (4%). The mean tumor volume was 16.3 cc (± 9.64, range: 1.85–32.56 cc) (Table 1).

Table 1: Characteristics of 26 benign meningioma patients.

	No.	%
Age:		
Mean (± SD)	54 years (± 10.5)	
Range	25–75 years	
Sex:		
Male	10	38%
Female	16	62%
Indication for SRS:		
Residual tumor	14	54%
Recurrent tumor	3	11.5%
Medical problems	4	15%
Old age <65 Years	3	8%
Multiple lesions	2	
Location of lesion:		
Skull base	19	73%
Tentorium	2	8%
Falcine/parasagital	4	15%
Convexity	1	4%
Tumor volume: Mean ± SD (Range)	16.3 cc± 9.64, (1.85–32.56 cc)	

The mean tumor dose at the tumor margin (prescribed at the 80% isodose line) was 17 Gy (± 2.9, range: 13 - 24Gy). Prescribed dose was given in a single or multiple fractions. 23 patients (88.5%) received single fraction, and three patients (11.5%) received two fractions. The prescribed dose was achieved using single isocentre in 16 patients (62%), 2 isocentres in 6 patients (23%) and three isocentres in four patients (15%). Collimator diameters ranged from 5 to 35mm (Table 2). All patients tolerated treatment well. The mean follow up period was 28 ± 8.15 months (range: 11– 42 months).

Table 2: Stereotactic radiosurgery treatment of 26 benign meningioma patients.

	No.	%
Tumor Margin Dose (80% isodose line):		
Mean (± SD)	17 Gy (± 2.9)	
Range	13 – 24 Gy	
Number of Fractions:		
Single	23	88.5%
Two	3	11.5%
Number of Isocentres:		
Single	16	62%
Two	6	23%
Three	4	15%

Tumor control was achieved in 23 patients (88.5 %) with tumor shrinkage in three patients (11.5 %) and stable tumor size in 20 patients (79%). Tumor progression occurred in three patients (11.5%). Radiological tumor control occurred in 23 patients (88.5%), who included tumor shrinkage in three patients (11.5 %) (Figure.1), and stable tumor size in 20 patients (79 %). Tumor progression occurred in three patients (11.5 %).

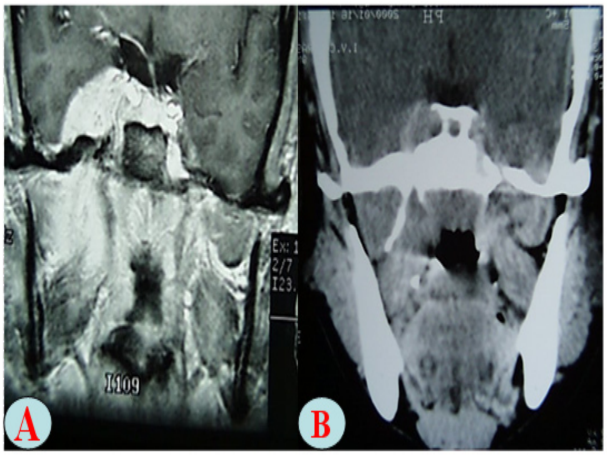

Fig. 1: Female patient, 47 years with right cavernous sinus meningiomas. **A:** Before stereotactic radiosurgery **B:** 16 months after stereotactic radiosurgery: Tumor shrinkage with decrease of enhancement.

Treatment complications included trigeminal and facial neuropathy in two patients (8%), and transient perifocal edema in three patients (12%). The remainders of the patients were clinically unchanged during the follow-up interval (Table 3).

Table 3: Clinical outcome of 26 benign meningioma patients.

	No.	%
Clinical Assessment:	26	100%
Overall clinical control	23	88.5%
Clinical response	3	11.5%
Stable disease	20	77%
Clinical deterioration		
No response	3	11.5%
Radiological Assessment:		
Tumor control	23	88.5%
Tumor shrinkage	3	11.5%
Stable tumor size	20	77%
Tumor progression	3	11.5%
Treatment Complications:		
Neuropathy	2	8%
Perifocal Edema	3	11.5%

DISCUSSIONS

Meningiomas are the most common benign intracranial tumors. They are usually diagnosed in middle age, and are significantly more frequent in females than in males[1,2]. Occasionally, treatment of meningioma represents a major challenge to both neurosurgeons and radiation oncologists. Some are locally invasive in the surrounding critical structure. The current treatment of choice is complete surgical resection, which may be difficult without significant morbidity[4]. The risk of recurrence is substantially greater after subtotal resection without adjuvant therapy. The five year survival rate after complete excision was 88% compared with 46% after subtotal excision[14]. Conventional postoperative radiation therapy significantly decreases rate of recurrence and prolong recurrence disease survival of meningioma patients who underwent subtotal surgical resection (30% and 125 months, respectively) compared to patients who didn't receive postoperative radiation therapy (60 % and 66 months, respectively, $P<0.05$)[7]. Similar results are reported by Taylor et al.[8] However its role is limited by the presence of radiosensitive normal structure close to these tumors[3,4,7,8].

SRS was originally introduced by Lars Leksell[15]. It has developed quite rapidly over the last decade mainly due to developments in 3-D imaging modalities, developments in 3-D and conformal planning systems, stringent quality assurance measures of target volume localization and safe dose delivery to the target volume[9].

It has emerged as a promising tool for treatment of brain tumor either to supplement subtotal surgical resection or as an alternative to open surgery in high-risk patients. It allows safe delivery of a high radiation dose to stereotactically defined target volume using single (SRS) or multiple fractions (stereotactic radiotherapy)[6, 10, 11].

Several reports have been published regarding the use of SRS in the treatment of meningioma[2, 10, 11,16-19]. Valentino et al. reported the results of SRS treatment of 72 middle fossa meningiomas with doses of 15 to 45Gy. Sixty nine percent of patients showed tumor shrinkage, 25% had no change and 6% had tumor progression. There were no significant treatment related complications[11]. Similar results were reported by Shafron et al.[2] in 76 meningiomas, Kondziolka et al.[19] in a large series of benign intracranial tumors including 85 meningioma patients and Flickinger et al.[17] in 219 meningioma patients. SRS is also preferable to re-operation, is indicated after incomplete surgical excision and is an excellent alternative to surgery in high-risk or elderly patients, and meningiomas infiltrating critical structures[20, 21, 11].

The optimal treatment dose required for meningiomas is uncertain, however, doses of 12-20Gy to the tumor margin are the most commonly employed since higher dosages have been associated with higher rates of morbidity[16]. The selection criteria, treatment dose and overall tumor control rate of the present series (89.5%) is comparable to that reported in the literatures[2, 11, 16, 17, 19-22].

Immediate side effects of SRS are usually mild to moderate and are mostly self-limited. Kalapurakal et al.[23] studied factors influencing cerebral edema after stereotactic radiosurgery or radiation therapy in intracranial meningiomas. The statistically significant factors for the development of edema were parasagittal location, presence of pretreatment edema, sagittal sinus occlusion, and the use of more than 6Gy per fraction. A smaller dose per fraction and aggressive use of steroids may prevent life-threatening complications due to worsening edema. Similar findings were reported by Gelblum et al.[24] and Singh et al.[25] However, the presence of pretreatment edema was not a predictor of post SRS complication rates in their series. The occurrence of edema did not correlate with tumor volume, margin or maximum dose, or with radiation received by adjacent brain[24, 25].

Complications of SRS include facial and trigeminal neuropathy, and perifocal edema. Two patients (8%) of this study developed facial and trigeminal neuropathy, which is lower than that reported by Friedman et al. (21%)[26] and higher than that reported by Steiner et al. (6%)[27]. Both patients were responded to medical treatment. Development of cranial nerve neuropathy is mainly determined by length of the nerve irradiated, degree of stretch of the nerve over the tumor and radiation dose[28]. Patients receiving a minimal tumor dose of <16Gy are at lower risk for permanent facial neuropathy after SRS. Perifocal edema developed in three patients (11.5%) of our series. Noren[28] reported it in 5% that involve the cerebellum and brain stem.

CONCLUSIONS

Despite technical advanced and growing experience in the past two decades, surgery of intracranial meningioma is not applicable all the times for all patients. SRS has emerged as an established treatment modality, which can supplement subtotal surgical resection of sizable or locally invasive tumors. It can be used as an alternative to surgery for recurrent tumors, inaccessible tumor sites especially skull base, for patients who have severe systemic illness or those who refuse to have open surgery. This treatment modality is well tolerated, has few complications, and induces good tumor control. More clinical trials and data analysis are needed to maximize its efficacy, to identify prognostic factors for better patient's selection, and to optimize dose of SRS for meningiomas.

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