Stereotactic radiosurgery and radiotherapy in benign intracranial meningioma

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Received 12 May 2011; accepted 21 June 2011
Available online 22 October 2011

Keywords: Stereotactic; Radiosurgery; Meningioma; Hypo-fractionated; Benign

Abstract  Purpose: To investigate the role of stereotactic radio surgery (SRS) and hypo-fractionated stereotactic radiotherapy (SRT) in treatment of benign intracranial meningioma.

Patients and methods: Between 2003 and 2010, 32 patients with a median age of 44 years (range 21–67 years) were treated with SRS (n = 19), and hypo-fractionated SRT (n = 13) for intracranial meningioma. Fourteen patients underwent SRS or SRT as their primary treatment, while 18 patients underwent post operative SRS or SRT (PORT). Cumulative progression free survival, overall cumulative survival, toxicity and symptomatology were evaluated.

Results: The median follow up period was 39 months (range 6–72 months). The 5 year overall survival and progression free survival were 90 ± 5% and 94 ± 4% after SRT or SRS respectively. Symptoms were improved or stable in 94% of patients. Acute toxicity was mild, and was seen in 41% of patients. Clinically significant late morbidity or new cranial nerve palsies did not occur.

Conclusion: Stereotactic radio surgery (SRS) and hypo-fractionated stereotactic radiotherapy (SRT) are effective and safe treatment modality for local control of meningioma with low risk of significant late toxicity. In case of large tumor size and adjacent critical structures, hypo-fractionated SRT is highly recommended.

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Introduction

Meningioma is the most common primary brain tumors, accounting for approximately 14–20% of non-glial brain tumors. Although they are usually benign, they can be associated with significant morbidity when encroaching on sensitive structures such as cranial nerves [1,2].

Surgery remains the mainstay of treatment with excellent local control, but may be limited by the size and site of tumor. The risk of cranial nerve palsies and other morbidities remains significant despite recent advances in microsurgical techniques [3].
Post operative radiotherapy (PORT) after subtotal resection has the potential to improve outcome and to increase survival rates [4,5]. In order to reduce radiation induced side effects and to increase local control, sophisticated treatment planning like stereotactic fractionated radiotherapy (SRT), stereotactic radiosurgery (SRS) and intensity modulated radiotherapy is recommended [6–8]. These techniques have enabled improved conformity of the treatment volume to the target, which is often small, of complex shape, and close to critical structures such as the brain stem, pituitary, and optic chiasma.

The aim of this work is to report our experience with stereotactic radiosurgery (SRS) and hypo-fractionated stereotactic radiotherapy (SRT) in the treatment of benign meningiomas with respect to local control, radiation-induced side effects, and overall survival.

Patients and methods

This is a retrospective study of 32 patients with intracranial benign meningioma who were treated with stereotactic radiosurgery (SRS) (19 patients), and hypo-fractionated stereotactic radiotherapy (SRT) (13 patients) during the period from 2003 to 2010 at the National Cancer Institute, Cairo university, Egypt.

All patients were evaluated before treatment by MRI. Maximal tumor diameter, tumor volume and distance to critical neural structures (optic pathway or brain stem) were assessed in all cases. Tumor with radiological well defined lesion, small volume (approximately less than 20 cc) and away from critical structures were candidates for stereotactic radiosurgery. Lesions with large volume and/or involving (or adjacent to) critical structures (brain stem and optic chiasma) were treated with hypo-fractionated SRT. The Karnofsky performance status (KPS) was recorded at the beginning of treatment and during follow up.

Treatment methods

Patient immobilization was achieved using Brown–Roberts–Wells (BRW) stereotactic localization frame in SRS, and Gill–Thomas–Cosmin (GTC) frame in hypo-fractionated SRT with repositioning accuracy <2 mm according to published data [9,10].

Treatment planning was performed on a three-dimensional CT data generated from continuous 2-mm CT scans. MRI scans were obtained in the treatment position. CT and MRI fusion was carried out using the three-dimensional planning system Radionics (X-Knife version 2). After stereotactic image fusion, the target volume and organs at risk, such as the eyes, optic nerves, chiasma and brain stem, were delineated on each slice of the three dimensional data. The planning target volume included the macroscopic tumor visible on MRI with a safety margin 2 mm in hypo-fractionated stereotactic radiotherapy (SRT) and no margin in stereotactic radiosurgery (SRS). Optimal dose distribution within the target volume and minimal dose to normal brain and critical structures were achieved with fixed non coplanar beams using either multi leaf collimator (leaf width 2 mm at the isocenter) or cones with different sizes. Treatment was delivered with 6 MV linear accelerator. The tumor margin dose was 11-12 GY in SRS patients and 2520 cGY in 6 fractions in hypo-fractionated SRT (equivalent to 30 GY/25 F/calculated for x/β = 2). Evaluation of treatment planning was carried out by isodose line distribution, dose volume histogram and target dose conformity. The prescription isodose volume to target volume ratio (PITV) is used by the Radiation Therapy Oncology Group (RTOG) to describe the conformity of prescription isodose line to the target volume. An exemplary treatment plan with beam’s eye view is shown in Fig. 1.

Follow up included radiologic (CT/MRI), clinical and neurologic examinations at 3 and 6 months after radiotherapy, then once a year. Radiologic tumor response was assessed after exact image fusion and measured volumetrically by use of fused thin slice MRI data sets. Tumor volume shrinkage was analyzed three dimensionally and quantitatively by use of planning system. If this procedure was not available, the tumor diameters were compared in 3 dimensions. Ophthalmologic examination and visual field perimetry in sellar and parasellar meningioma was performed after 6 months and then annually after radiotherapy. Side effects were assessed as either acute or late phenomena according to the Radiation Therapy Oncology Group (RTOG) morbidity criteria [11]. A toxic effect was considered to be acute if it occurred within the first 90 days after start of treatment, and was considered late if it occurred after 90 days from the start of treatment.

Overall survival was calculated from the date of starting radiotherapy until the date of death or the date of last follow up, and progression free survival was calculated from the date of starting radiotherapy until the date of first progression or the date of last follow up.

Statistical methods

Statistical analysis was done using SPSS win statistical package version 15, estimates of the survival rates (cumulative overall survival and progression free survival) were calculated using the Kaplan–Meier product-limit method and presented as cumulative survival and standard error at the end of follow up period.

Results

They were 25 female patients and 7 males. The median age was 44 years (range 21–67 years). Fourteen patients underwent SRS or SRT as their primary treatment while 18 patients underwent post operative SRS or SRT. The histological or radiological diagnosis of benign meningioma was confirmed in all patients. Table 1 shows the patients characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median 44 (range 21–67)</td>
</tr>
<tr>
<td>Gender</td>
<td>25 females, 7 males</td>
</tr>
<tr>
<td>Treatment type</td>
<td>14 SRS, 18 SRT</td>
</tr>
<tr>
<td>Survival</td>
<td>Overall survival and progression free survival calculated</td>
</tr>
</tbody>
</table>

Follow up period was 39 months (range 6–72 months). Symptoms of increased intracranial pressure (headache, vomiting and blurring of vision) were the most commonly encountered seen in 75% (24/32) of the patients, followed by neurological deficits (motor weakness, impaired sensation and nerve affection) detected in 63% (20/32) of the patients. Convulsion was encountered in 22% (7/32 patients), while hormone deficit was seen in 6% (2/32) of the patients. All patients were (KPS) more than 70. In 31% (10/32) of the patients, preexisting neurologic symptoms improved, 63% (20/32) remained unchanged and 6% (two patients) get worse.

Table 2 shows the distribution of 32 patients according to the site of the lesions. Sellar and parasellar lesions were the most common (31%) followed by lobar lesions (28%). The total number of all treated lesions was 36 lesions. The tumor volume ranged from 1 to 39.7 cc, with a median of 8.5 cc. Dose delivery was normalized to isodose line ranged...
from 55% to 94%, the median being 85% isodose line. The volume of lesion covered with the prescribed dose ranged from 86% to 99.5%, the median being 94%. The number of nonco-planar arcs ranged from 4 to 17 arcs, the median being 6 arcs. All patients were treated with PITV ratio less than 2 (Fig. 2).

Stable disease based on MRI was seen in 20/32 (63%) patients, while 10/32 (31%) patients had a reduction of tumor volume of >50% and 2/32 (6%) patient had a progression of tumor volume of >25% during follow up period. Two patients died 6 and 7 months after end of treatment due to cardiac failure while one patient died from disease progression 32 months after end of treatment. The cumulative overall survival rate for the whole group was 90 ± 5% at 5 years, (Fig. 3). Overall tumor growth control at the last follow up was observed in 30 patients. Cumulative progression free survival (PFS) at 5 years was 94 ± 4%, (Fig. 4). Two patients exhibited tumor progression; both of them had parasellar meningioma.

Acute toxicity was mild and consisted of mild headache, transient tinnitus or general weakness in 8/32 (25%) patients. Short term course of corticosteroids therapy (<3 months)
was given to 3/32 (9.3%) patients. Visual field deterioration was seen in 2/32 (6.2%) patients, one of them was due to disease progression. No patient developed hypothalamic–pituitary dysfunction. No sign of increased intracranial pressure due to post radiation therapy oedema was detected in our patients. No late toxicity was detected within the follow up period.

Discussion

An increasing number of reports concerning SRS and SRT as an adjuvant treatment or as an alternative therapy to aggressive microsurgery have been published. SRT given after incomplete resection of primary or recurrent meningioma or as first line treatment has been shown to improve tumor control compared with outcomes in patients treated by surgery alone [12–17].

More recently, several studies have reported encouraging results on SRS treatment for benign meningioma. Despite the objections raised after the publications of preliminary results of this technique, long term evaluation of SRS in meningioma treatment has demonstrated an improved tumor control whether used as first line or post resection adjuvant treatment [18–20].

The 5 year PFS rate for 32 patients with benign meningioma treated by SRS and SRT in our department was 94%. These data are nearly comparable with other reports [21–25]. Selch et al. reported a 3-year progression free survival of 97.4% in 45 patients treated for benign meningiomas with fractionated stereotactic radiotherapy [21]. Jalali et al. with a median follow up of 21 months has reported no recurrences in 41 patients treated with SRT [22]. The largest study to date was introduced by Debus et al. A total number of 189 patients treated with fractionated stereotactic radiotherapy with a median follow up of 35 months have been followed; local control was excellent, with only 3 patients recurring [23].

Single fraction stereotactic radiosurgery has also been used extensively to treat skull base meningiomas with similar high levels of local control. Lee et al. reported a series of 159 patients with cavernous sinus meningiomas treated with gamma knife radiosurgery showing local control of 93% with a median follow up of 35 months [24]. Shafron et al. treated 70 benign meningiomas with a mean follow up of 23 months showing a 100% control rate [25].

Our results are better than the results achieved in microsurgical series with available follow up [26–28]. In the two principal microsurgical series, the PFS rate ranged from 61.5% to 80.7% with a mean follow up inferior to 4 year [26,27].

On the basis of different definitions and preconditions, the data for radiologic tumor response is very heterogeneous. Tumor volume shrinkage was published between 13% and 61% [29–32]. If not measured volumetrically (by use of fused thin slice MRI data sets), the interpretation of these results appears to be very difficult. Most of the authors define regression as 2 mm shrinkage in tumor diameter, but to have MRI images with exactly the same slice angulations available is rare, even though they are needed for exact comparison [33,34]. In our patient group, in respect to our definition of tumor volume shrinkage/enlargement, tumor shrinkage (reduction of tumor volume of >50%) was observed in 31% of patients.

In comparing our study to those of other authors, we observed an unchanged (63%) and improved (31%) clinical status. Only 2 of 32 patients (6%) showed worsening conditions. Higher [33,34] and lower [25,31,32] worsening rates were published.

Conclusion

SRS and SRT are effective and safe treatment modality for local control of meningioma with low risk of significant acute and late toxicity. In case of large tumor size and adjacent critical structures SRT is highly recommended.
References