The Role of Radiotherapy in the Management of Intracranial Meningiomas

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ABSTRACT

Introduction: Cerebral meningiomas account for 15–20% of all cerebral tumors. Although seldom malignant, they frequently recur in spite of complete surgery, which remains the cornerstone of the treatment. In order to decrease the probability of local recurrence, radiotherapy has often been recommended in atypical or malignant meningioma as well as in benign meningioma which was incompletely resected. However, this treatment never was the subject of prospective studies, randomized or not. Methods: We retrospectively reviewed all patients with meningioma treated with radiotherapy in the oncology department of Hospital University Mohammed 6 in Marrakech from 1 January 2011 to 1 December 2014. Demographic data including age, sex, and clinical signs revealing meningioma been studied. All patients in the study received surgical treatment and radiotherapy. The histological data of the surgical specimens have been studied, neurological evolution and therapeutic complications were analyzed. Results: From January 2011 to December 2014, six patients were identified with a median age of 43.5 years (range 25-56 years). Sex-ratio was 0.5. Headache was the most common presenting symptom manifesting in 4 patients (66.6%). Tumors were mostly located in the convexity (83.3%). Five patients underwent complete excision (Simpson I à III) and 1 underwent subtotal excision (Simpson IV). On histopathological analysis, 2 patients (33.3%) had WHO grade I, 2 patients (33.3%) had WHO grade II (atypical) and 2 patients (33.3%) grade III. 4 patients had adjuvant radiation from initial management and 2 patients with grade I meningioma had adjuvant radiotherapy after recurrence and surgical reoperation. For evolution, a tumor recurrence was observed at control imaging in the 12th months, the disease was stabilized for the patient with sphenoorbital localization, for the remaining four patients, the disease was controlled. No grade 3 or 4 toxicity were observed. Conclusion: Adjuvant radiotherapy improved local control after incomplete resection for grade I meningiomas, and after complete resection for high-grade meningiomas.

Keywords: Intracranial, Meningioma, Surgery, Radiation Therapy

1. INTRODUCTION

Intracranial Meningiomas are the second most common tumor of the central nervous system, accounting for 15–20% of all primary brain tumors in adults (1). The high-risk tumors are classified as atypical (World Health Organization [WHO] grade II) or anaplastic (WHO grade III) meningiomas. Their quoted incidence varies widely from 1.5% to 35% of all meningiomas, largely related to inconsistencies in histopathologic grading (2–3). While the extent of resection is an important prognostic factor (4), gross total resection (GTR) may not be sufficient for long-term disease control of atypical meningiomas. Radiotherapy may be employed postoperatively (early adjuvant), though its use is supported.

by only weak evidence, consisting of small retrospective case series with conflicting results\textsuperscript{(5,6)}. We herein report our institutional experience of 6 patients with intracranial meningiomas treated from 2011 to 2014.

2. METHODS

We retrospectively reviewed the patients of intracranial meningiomas from January 2011 to December 2014 treated in our institute. The total number of patients was 6. We reviewed the record of these patients to extract the following information: Age, sex, clinical symptoms, histology, radiology (computed tomography/magnetic resonance imaging (CT/MRI)), tumor extent, extent of surgical resection, radiation (technique, total dose, dose per fraction, and number of fractions), toxicity, response, recurrence, progression, and death.

3. RESULTS

Between January 2011 and December 2014, six patients with intracranial meningioma were registered in our department. The median age of the patients was 43.5 years and ranges from 25 to 56 years. 02 patients (33.3%) were males and four patients (66.6%) were females, sex ratio was 0.5. The tumor was located at the convexity in 5 patients (83.3%), and sphenoorbital in one patient (Figures 1,2,3,4).

![Fig. 1 & 2: Axial cerebral Ct scan showing a left parietal convexity meningioma](image1)

![Fig. 3 & 4: Axial and sagittal cerebral MRI showing a process of left parietal convexity compatible with a meningioma](image2)
The median duration of symptoms was seven months. Headache was the most common presenting symptom manifesting in 4 patients (66.6%) followed by vomiting, seizures, motor weakness (50%), and blindness in one patient. On histopathological analysis, two patients (33.3%) had WHO grade I, two patients (33.3%) had WHO grade II (atypical) and two patients (33.3%) grade III.

Treatment modalities consisted of surgery and radiotherapy. All patients underwent primary surgery, out of which five patients underwent complete excision (Simpson I à III), and 1 underwent subtotal excision (Simpson IV). 2 patients had a tumor recurrence with an average delay of 30 months, they underwent a re-intervention associated with adjuvant radiotherapy. Four patients had an adjuvant irradiation from the initial management.

For RT planning, gross tumor volume (GTV) was defined as the macroscopic lesion visible on the contrast-enhanced imaging and/or the resection cavity. Clinical target volume (CTV) was defined by adding 1–2 cm margin to GTV adhering to anatomical borders. The planning target volume (PTV) was calculated from the CTV using a uniform 3D expansion of 0.5 cm. Early postoperative RT was delivered in 4 patients, and the other two patients received RT after progression of the disease. Median RT dose was 54.0 Gy which ranged from 50 to 60 Gy. For evolution, a tumor recurrence was observed at control imaging in the 12th month (grade III), the disease was stabilized for the patient with sphenoorbital localization (grade II), and for the remaining four patients, the disease was controlled. No grade 3 or 4 toxicity were observed. Grade 2 radiotherapy toxicities included a headache, alopecia and memory impairment were observed in three patients, Grade 1 radiation-related toxicities included fatigue and headache were observed in two patients. There were no Grade 3 or 4 toxicities attributed to radiotherapy in our patients.

4. DISCUSSION

Intracranial Meningiomas are the second most common tumor of the central nervous system, accounting for 15–20% of all primary brain tumors in adults(7). The World Health Organization (WHO) 2007 classification system classifies meningiomas into three grades, I-III. Most of the meningiomas are of low risk, and only a minority of around 10% is graded as high-risk tumors. These high-risk tumors are atypical and malignant meningiomas comprising 5–7% and 1–3%, respectively, of all meningiomas.(7,8)

The most common locations of meningiomas, in descending order of frequency, are convexity (19–34%), parasagittal (18–25%), sphenoid and middle cranial fossa (17–25%), frontal base (10%) and posterior fossa (9–15%), cerebellar convexity (5%), cerebellopontine angle (2–4%), intraventricular (1–5%), and clivus (1%).

Therapy for patients with meningioma needs to be individualized because the nature of meningiomas and the potential consequences of different treatments for different patients vary greatly. If therapy is needed for radiologically confirmed growth or the presence of clinical symptoms, surgery is the first choice. The extent of resection has long been known to influence the likelihood of recurrence in meningiomas. The Simpson grade is the established system, although some have recently challenged its prognostic value in the modern neurosurgical era. In WHO Grade I meningioma, Sunghrue et al. found no statistically significant difference in tumor recurrence rates according to Simpson grade, though gross figures suggest otherwise (5 years PFS 95% versus 81% for Grade I and IV, respectively)(10). Indeed, grouping Simpson grades together into categories of gross tumor resection and subtotal resection results in a better prognostic value(11,12), and these definitions have been adopted by the European Organisation for Research and Treatment of Cancer (EORTC) and European Organisation for Research and Treatment of Cancer (RTOG).

The routine use of adjuvant radiotherapy following resection of atypical meningiomas (AMs) is controversial because although some series demonstrate that the addition of radiotherapy is an independent predictor of improved PFS(13,14,15). Others dispute this finding and recommend against the routine use of adjuvant radiotherapy(16,17,18). For patients who have a subtotal resection (STR) or biopsy, adjuvant radiation treatment provides an improved progression-free survival as indicated by several studies(19,20). Generally, the use of adjuvant fractionated external beam RT (EBRT) or stereotactic radiosurgery (SRS) after STR for both atypical and anaplastic meningiomas is accepted in the neurosurgical community due to the high recurrence rate after surgery alone.

Current guidelines of the National Comprehensive Cancer Network recommend GTR alone for accessible tumors with adjuvant RT reserved for incomplete resections or recurrences for both atypical and WHO meningioma.
grade I meningiomas. However, because of the increased risk for disease relapse in atypical meningiomas in up to 30% of cases, even after GTR, the management paradigm for these lesions recently has been contended. The most recent study evaluating RT in anaplastic meningiomas was done in 2010 and recommends radiotherapy after all surgical resections.

Moreover, not only the indication for RT is influenced by histology, but also target volume definition and the RT dose. For high-grade tumors. Larger safety margins are required than for WHO grade I tumors. For grade II tumors, the CTV includes a 1–2 cm safety margin, while for grade III tumors 2–3 cm safety margin for CTV is recommended. Similarly, RT doses for grade II tumors is 50–54 Gy and for grade III tumors is 54–60 Gy.

Radiosurgery may be used for patients who have recurrent or residual tumors or as a primary treatment in patients unwilling or unable to undergo surgery and who possess a lesion with the typical imaging characteristics of a meningioma. Radiosurgery for Meningiomas is usually performed with the gamma knife (GK).

For treatment of refractory atypical and anaplastic meningiomas with aggressive pathologic features, pharmacologic treatment is occasionally necessary. Several clinical trials investigating the benefit of immunotherapeutic and hormonal agents have been performed with a minimal benefit.

5. CONCLUSION

The management of meningiomas is a paradigm of cooperation between clinicians, surgeons, and pathologists from establishing diagnosis to organizing the therapeutic strategy. Postoperative adjuvant radiotherapy should be offered to all patients with high risk meningiomas, regardless of the degree of resection achieved, given the high rate of local recurrences. Novel strategies including advanced RT techniques such as intensity modulated RT (IMRT), stereotactic radiosurgery (SRS), stereotactic RT (SRT), and proton therapy should be prospectively investigated.

REFERENCES