Clinical Neurology and Neurosurgery 128 (2015) 112–116

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Skull base atypical meningioma: Long term surgical outcome and prognostic factors

Yu-Chi Wang[a], Chi-Cheng Chuang[a], Kuo-Chen Wei[a], Yung-Hsin Hsu[a], Peng-Wei Hsu[a], Shih-Tseng Lee[a], Chieh-Tsai Wu[a], Chen-Kan Tseng[b], Chun-Chieh Wang[b], Yao-Liang Chen[c], Shih-Min Jung[d], Pin-Yuan Chen[a,*]

[a] Department of Neurosurgery, Chang Gung Memorial Hospital at Linkou, Chang Gung University, Taoyuan, Taiwan, ROC
[b] Department of Radiation Oncology, Chang Gung Memorial Hospital at Linkou, Chang Gung University, Taoyuan, Taiwan, ROC
[c] Department of Radiology, Chang Gung Memorial Hospital at Linkou, Chang Gung University, Taoyuan, Taiwan, ROC
[d] Department of Pathology, Chang Gung Memorial Hospital at Linkou, Chang Gung University, Taoyuan, Taiwan, ROC

ARTICLE INFO

Article history:
Received 18 September 2014
Received in revised form 2 November 2014
Accepted 10 November 2014
Available online 24 November 2014

Keywords:
Atypical meningioma
Skull base
Surgery
Radiotherapy
MIB-1 index

ABSTRACT

Purpose: The aim of this study was to examine the clinical outcomes of treating atypical meningioma at the skull base region following surgical resection and adjuvant radiotherapy, and to analyze the association between clinical characteristics and progression free survival.
Materials and methods: Twenty-eight patients with skull base atypical meningiomas underwent microsurgical resection between June 2001 and November 2009. The clinical characteristics of the patients and meningiomas, the extent of surgical resection, and complications after treatment were retrospectively analyzed.
Results: Thirteen patients (46.4%) had disease recurrence or progression during follow up time. The median time to disease progression was 64 months. The extent of the surgical resection significantly impacted prognosis. Gross total resection (GTR) of the tumor improved progression free survival (PFS) compared to subtotal resection (STR, $p = 0.011$). An older patient age at diagnosis also resulted in a worse outcome ($p = 0.024$). An MIB-1 index <8% also contributed to improved PFS ($p = 0.031$). None of the patients that underwent GTR and received adjuvant radiotherapy had tumors recur during follow up. STR with adjuvant radiotherapy tended to result in better local tumor control than STR alone ($p = 0.074$). Three of 28 patients (10.7%) developed complications after microsurgery. The GTR group had a higher rate of complications than those with STR. There were no late adverse effects after adjuvant radiotherapy during follow up.
Conclusion: For patients with skull base atypical meningiomas, GTR is desirable for longer PFS, unless radical excision is expected to lead to severe complications. Adjuvant radiation therapy is advisable to reduce tumor recurrence regardless of the extent of surgical resection. Age of disease onset and the MIB-1 index of the tumor were both independent prognostic factors of clinical outcome.

1. Introduction

Meningiomas are neoplasms that develop from the arachnoid cap cells of the central nervous system (CNS) [1]. They are graded histologically using standards released by the World Health Organization (WHO) in 2000 and 2007, which are based on a combination of objective (mitotic index) and subjective criteria [2]. Approximately 90% of meningiomas are classified as benign, 5–7% as atypical, and only 1–3% are considered malignant [3].

About 30% of meningiomas develop at the skull base [4]. Skull base meningiomas frequently lead to serious and potentially lethal consequences because of their intracranial location, regardless of the pathological type [5]. On the other hand, compared to the relatively good prognosis for benign meningiomas, atypical meningiomas are more locally aggressive and progress more rapidly. Previous studies have shown 5-year recurrence rates of approximately 40% for atypical meningiomas [1,6,7]. Gross total removal (GTR) is the accepted standard of care for benign meningiomas, but the optimal surgical management for atypical meningiomas has yet to be established, especially at skull base area [8,9]. In addition,

* Corresponding author at: Department of Neurosurgery, Chang Gung Memorial Hospital, #5, Fu-Hsing St., Kweishan, Taoyuan 33305, Taiwan.
Tel.: +886 3 328 1200x2412; fax: +886 3 328 5818.
E-mail address: pinyuanc@gmail.com (P.-Y. Chen).

http://dx.doi.org/10.1016/j.clineuro.2014.11.009
0303-8467/

the role of adjuvant radiotherapy and stereotatic radiosurgery after operating remains controversial [10–14].

In the meningiomas of this specific pathologic and anatomic field, prognostic factors and therapeutic strategy are unclear, and considerable controversy remains. To establish optimal treatment strategies, it is essential to accurately evaluate the risk factors for tumor progression in skull base atypical meningiomas. To understand the impact of surgical resection on the clinical outcome and the risk factor associated with atypical meningioma recurrence, we retrospectively analyzed the recurrence rate in a consecutive series of skull base atypical meningioma patients. In addition, we determined factors predicting tumor recurrence in this patient population.

2. Patients and methods

We retrospectively reviewed records for all of the patients that were treated for atypical meningioma between June 2001 and November 2009 at Chung Gang Memorial Hospital. This study was approved by the Chung Gang Memorial Hospital institutional review board.

The following clinical information was recorded for each patient: sex; age at diagnosis; tumor volume and location; operative characteristics; recurrence details; use of postoperative adjuvant radiotherapy; and the duration of follow up. Atypical meningiomas were diagnosed based on neuropathology using the 2007 WHO criteria. Current criteria were retrospectively applied to older histopathological sampling. Of the 96 patients with atypical meningioma evaluated, 35 patients had tumors located in the skull base area. Four patients with recurrent atypical meningioma after being treated previously for benign meningioma, or who multiple intracranial meningiomas were excluded because of the difficulty in evaluating the treatment response. Other three patients were either lost to follow-up or had incomplete records and were excluded from this evaluation, leaving 28 patients for final analysis.

2.1. Patient population and tumor characteristics

The current study included 13 male and 15 female patients. The mean age of the group at the time the initial surgery was performed was 56.8 years and ranged between 23 and 85 years. Skull base tumors were divided into five categories according to the anatomic location: (1) sphenoid ridge ($n = 11$); (2) olfactory groove ($n = 3$); (3) sella ($n = 4$); (4) petroclivus ($n = 6$); and (5) other areas ($n = 4$). Immunohistochemical evaluation was performed using anti-Ki 67 antibody, and the MIB-1 index is the percentage of cells reactive for Ki 67. It was determined by counting tumor cell nuclei of 1000 tumor cell nuclei evaluated in at least three high magnification (400×) vision fields. The index was available for 25 tumor specimens and ranged from 2% to 25%, with an average of 8.6%.(Table 1).

2.2. Treatment methods

All patients underwent an initial microsurgical resection after diagnosis of atypical meningioma. The surgery was classified as a GTR or not based on the surgeon's impression intraoperatively and the postoperative MRI results. GTR was achieved in 14 patients (50%), while the other 14 patients (50%) underwent subtotal resection (STR) to treat their tumors. Radiotherapy was used in 12 out of 28 (42.9%) patients following surgical intervention. The remaining 16 patients (57.1%) did not receive adjuvant radiotherapy treatment. The total radiation dose was 54–60 Gy, delivered in 27–30 fractions. All adjuvant radiotherapy was given within 6 months of surgery, and before any clinical or radiographic signs of tumor recurrence.

Table 1
Patient demographics and tumor characteristics.

	Number (%)	Surgical resection	
		Gross total	Subtotal
All patients	28	14	14
Gender			
Male	13(46.4)	7	6
Female	15(53.6)	7	8
Age			
Mean ± SD	56.7 ± 2.5	53.6 ± 3.9	59.9 ± 3.2
Location			
Sphenoid ridge	11(39.3)	6	5
Olfactory groove	3(10.7)	1	2
Sella region	4(14.3)	2	2
Petroclivus	6(21.4)	3	3
Others	4(14.3)	2	2
Adjuvant RT			
Yes	12(42.9)	3	9
No	16(57.1)	11	5
MIB-1 index			
Mean	8.6	8.9	8.1
Recurrence or progression			
Yes	13 (46.4)	4	9
No	15 (53.6)	10	5

2.3. Follow up evaluation

The mean follow-up time was 57.4 months (range: 16–144 months). Disease progression, defined as recurred tumors after GTR or enlarged residual tumor after STR, were assessed using radiological evidence from Gd-enhanced MRI in all cases. Progression free survival (PFS) was calculated from the day of initial surgical treatment to the time of disease progression.

2.4. Statistical analysis

Statistical analysis was performed using SPSS software (version 19; SPSS Inc. IBM Corporation). PFS rates were calculated using the Kaplan–Meier method, and comparisons between groups were performed using log-rank tests. Univariate Cox proportional hazards models and multivariate Cox regression analyses were used to identify risk factors for recurrence. A p value < 0.05 was considered statistically significant.

3. Results

All 28 patients survived until the end of follow up, and the 5-year overall survival rate was 100%. However, during the follow up period, 13 patients (46.4%) had signs of tumor recurrence or enlargement. The median time to disease progression in these patients was 64 months (range: 3–86 months). One patient had distant metastasis to the thoracic spine with local recurrence (Table 1).

We used Cox proportional hazard and Cox regression analyses to determine which clinical variables likely contributed to tumor recurrence or progression. The extent of surgical resection status had a significant impact on PFS, 71.4% of the GTR patients were progression free compared to 35.7% of the STR patients ($p = 0.011$, Fig. 1). In contrast, there was no association between whether patients received adjuvant radiotherapy and PFS (Kaplan–Meier log-rank test; $p = 0.376$). An MIB-1 index >8% was also associated with a higher rate of progression ($p = 0.031$, Fig. 2). Sex did not contribute significantly to PFS, but age had a significant influence ($p = 0.024$). Neither the diameters nor the locations of the tumors were associated with disease progression. Upon multivariate analysis, only the completeness of the surgical resection and an MIB index <8% were associated with better PFS (Table 2). In the multivariate analysis, age was no longer significantly associated with PFS.