Int J Clin Exp Med 2014;7(12):5696-5700
www.ijcem.com /ISSN:1940-5901/IJCEM0002668

Original Article

The potential risk factors for atypical and anaplastic meningiomas: clinical series of 1,239 cases

Ruo-Fei Liang[1], Ying-Jie Xiu[2], Xiang Wang[1], Mao Li[1], Yuan Yang[1], Qing Mao[1], Yan-Hui Liu[1]

[1]Department of Neurosurgery, West China Hospital of Sichuan University, Chengdu, P. R. China; [2]Department of Pathology, West China Hospital of Sichuan university, Chengdu, P. R. China

Received September 21, 2014; Accepted November 25, 2014; Epub December 15, 2014; Published December 30, 2014

Abstract: Background: Determining factors that could accurately predict pathological features of meningiomas before histological diagnosis would help surgeons to proper balance the risk of operation and the resection grade. The aim of this study was to explore the potential risk factors for atypical (WHO Grade II) and anaplastic (WHO Grade III) meningiomas. Methods: Records of 1,239 patients between January 2009 and January 2013 were included in this research. Furthermore, immunohistochemistry with Ki67 was analysed in 368 samples. Results: The Pearson's chi-square test showed an increased risk for male gender for atypical and anaplastic meningiomas ($P < 0.001$) and an increased risk for cerebral convexity for atypical and anaplastic meningiomas ($P < 0.001$). However, significant differences in the terms of falx/sagittal sinus and intraventricular were not found. Patients with a Ki67 index ≥ 5% were significantly more likely to have atypical and anaplastic meningiomas than those patients with a Ki67 index < 5% ($P < 0.001$). In addition, the percentage of patients with a Ki67 index ≥ 5% in cerebral convexity meningiomas was higher than in non-cerebral convexity location ($P = 0.006$). Conclusions: The results indicate that male gender, cerebral convexity are significant risk factors for atypical and anaplastic meningiomas.

Keywords: Cerebral convexity, risk factor, meningiomas

Introduction

Meningiomas are slowly growing tumors, and represent the common intracranial neoplasms in adults [1]. About 90% of meningiomas are benign (Grade I), and 5-7% are atypical (Grade II), while 1-3% are anaplastic (Grade III) [2]. Benign meningiomas have the lowest rate of recurrence following surgery with or without additional radiotherapy [3], however, due to their aggressive behavior, atypical and anaplastic meningiomas have a higher rate of recurrence, despite underwent standard therapy (surgery and radiation). At present, the pathologic examination as the gold standard for diagnosing the meningiomas, whereas, for patients with small meningiomas, gamma knife surgery is considered as the initial treatment strategy, and once if they proved to be higher-grade pathology, further treatment becomes difficult [4]. Without a pathologic diagnosis, higher-grade tumors will be missed and treated with primary gamma knife surgery or observed inappropriately [5]. So, an understanding of the probability that a lesion is higher-grade pathology before treatment initiation may help guide treatment strategies.

The aim of this study was to explore the potential risk factors for atypical and anaplastic meningiomas from a single centre. In this retrospective study, a series of 1,239 meningiomas were included. They consist of 1,048 benign meningiomas and 191 atypical/anaplastic meningiomas diagnosed by histopathology.

Methods

Patients and tissue specimens

Patients who underwent a primary operation between January 2009 and January 2013 were included in this research. Patients who underwent prior radiotherapy were excluded from our study. Patients with spinal meningiomas and multiple meningiomas were also excluded from our study. As to patients with repeated resec-

Table 1. Clinical information of patients (n = 1,239)

Characteristic	Number	Value (%)
Gender		
Male	355	28.7
Female	884	71.3
Age (years)		
< 65	1,033	83.4
≥ 65	206	16.6
Tumor location		
Skull base	458	37.0
Cerebral convexity	572	46.2
Falx/sagittal sinus	57	4.6
Intraventricular	50	4.0
Other	102	8.2
Histology		
Benign	1,048	84.6
Atypical and anaplastic	191	15.4

tion, only the primary operation was collected in our data analysis. The information collected included gender, age, histology of the tumor, and location of the tumor.

Pathologic review

All meningiomas samples were assessed and graded according to the 2007 WHO guidelines [6]. The tissue in these cases was fixed in 4% buffered formalin, routinely processed, and embedded in paraffin; 2-4 μm thick sections were stained with hematoxylin and eosin. For 368 (29.7%) samples, representative sections of were stained immunohistochemically for Ki-67 (1:100, MAIXIN-BiO, Mouse monoclonal, clone: MIB1) by the method of Envision. The Ki67 proliferative index was determined by counting the number of Ki67-positive cells within at least 1000 tumor cells. In addition, the Ki67 index was analysed with a cut-off value of 5%.

Tumor location

The evaluation of anatomical location was based on radiological records and/or operation notes. The locations of the meningiomas were as follows: skull-base (n = 458), cerebral convexity (n = 572), falx/sagittal sinus (n = 57), intraventricular (n = 50) and other (n = 102). In order to facilitate statistical analysis, tumors located in the skull-base were assigned in the group of skull-base tumors, and the others in the group of non-skull-base tumors. Tumors located in the cerebral convexity were assigned in the group of cerebral convexity tumors, and the others in the group of non-cerebral convexity tumors. Tumors located in the falx/sagittal sinus were assigned in the group of falx/sagittal sinus tumors, and the others in the group of non-falx/sagittal sinus tumors. Tumors located in the intraventricular were assigned in the group of intraventricular tumors, and the others in the group of non-intraventricular tumors.

Table 2. The Pearson's chi-square test of potential risk factors for atypical and anaplastic meningiomas

Characteristic	No. of atypical and anaplastic	*P* value
Gender		
Male	77	< 0.001
Female	114	
Age (years)		
< 65	161	0.711
≥ 65	30	
Tumor location		
Skull base	36	< 0.001
Non-skull base	155	
Cerebral convexity	122	< 0.001
Non-cerebral convexity	69	
Falx/sagittal sinus	9	0.936
Non-falx/sagittal sinus	182	
Intraventricular	8	0.907
Non-intraventricular	183	

Statistical analysis

SPSS software (version 21.0, IBM) was used for statistical analysis. A *P*-value greater than 0.05 was treated as no statistical significance.

Results

A total of 1,239 patients were included in our study. The information of these patients was summarized in the **Table 1**. The results of the Pearson's chi-square test are listed in the **Table 2**.

There were 884 females and 355 males (female-male ratio, 2.5) included in this study. There were 77 males had atypical and anaplastic meningiomas, while 114 females had atypical and anaplastic meningiomas. The Pearson's

chi-square test showed an increased risk for male gender for atypical and anaplastic meningiomas (21.7% vs. 12.9%, $P < 0.001$).

The mean age of the patients was 51.76 years old, ranging from 0.4 to 85 years old. Patients with benign meningiomas and atypical/anaplastic meningiomas had about the same mean age (51.8 vs. 51.3 years; $P = 0.064$, *t*-test). The Pearson's chi-square test showed that there was no statistical significance between age < 65 years and age ≥ 65 years for atypical and anaplastic meningiomas (15.6% vs. 14.6%, $P = 0.711$).

The most common site of atypical and anaplastic meningiomas was the cerebral convexity (n = 122, 63.9%), followed by the skull base (n = 36, 18.9%), other (n = 16, 8.4%), the falx/sagittal sinus region (n = 9, 4.7%) and the intraventricular region (n = 8, 4.2%). The Pearson's chi-square test showed a decreased risk for skull base for atypical and anaplastic meningiomas (7.9% vs. 19.8%, $P < 0.001$). And an increased risk for cerebral convexity for atypical and anaplastic meningiomas (21.3% vs. 10.3%, $P < 0.001$). There was no statistical significance between the falx/sagittal sinus region and the non-falx/sagittal sinus region for atypical and anaplastic meningiomas (15.8% vs. 15.4%, $P = 0.936$, the Pearson's chi-square test). And there was no statistical significance between the intraventricular region and the non-intraventricular region for atypical and anaplastic meningiomas (16.0% vs. 15.4%, $P = 0.907$, the Pearson's chi-square test). The Ki67 index was obtainable in 368 (29.7%) cases. When analysed with a cut-off value of 5%, 203 (55.2%) cases were < 5% and 165 (44.8%) were ≥ 5%. Patients with a Ki67 index ≥ 5% were significantly more likely to have atypical and anaplastic meningiomas than those patients with a Ki67 index < 5% (49.7% vs. 6.9%, $P < 0.001$, the Pearson's chi-square test). In addition, the percentage of patients with a Ki67 index ≥ 5% in cerebral convexity meningiomas was higher than in non-cerebral convexity location (52.8% vs. 38.5%, $P = 0.006$, the Pearson's chi-square test).

Discussion

Determining factors that could accurately predict pathological features of meningiomas before histological diagnosis would help surgeons to proper balance the risk of operation and the resection grade. This is also critical for a non-invasive treatment modality. In this study, we stratified the case according to anatomical locations. The results indicate that male gender and cerebral convexity are significant risk factors for atypical and anaplastic meningiomas. Although female gender has an overall higher incidence of meningiomas [7, 8], our results showed an increased risk for male gender for higher-grade meningiomas which was according to the previous studies [4, 5, 9-15]. The possible reasons for the male gender association with higher-grade meningiomas are still unclear. The chromosome abnormalities, hormone receptor status and hormone levels might affect the trend for higher grade tumors [4].

In our study, patients with benign meningiomas and atypical/anaplastic meningiomas had about the same mean age (51.8 vs. 51.3 years; $P = 0.064$, *t*-test). This is in line with previous findings [16]. In contrast, Wang et al. [15] reported that the mean age of patients with higher-grade meningiomas was significantly lower than those with benign meningiomas. Based on prior studies [5, 10], we did not find that patients ≥ 65 years correlated positively with atypical and anaplastic meningiomas. Therefore, the relationship of age and meningioma grade is still controversial.

The observations that non-skull base meningiomas are more likely to be the higher-grade meningiomas is supported by many studies [4, 5, 10, 14]. This was also confirmed by our present study. Based on the further detailed anatomical stratification of non-skull base location, we found that the most common site of atypical and anaplastic meningiomas was the cerebral convexity. Based on the Pearson's chi-square test, we found that meningiomas with cerebral convexity location have an increased risk of atypical and anaplastic meningiomas. However, significant differences in the terms of falx/sagittal sinus and intraventricular were not found. Furthermore, we found the Ki67 index significant increased with the grade of meningiomas, this is in line with previous study [17]. Additionally, the percentage of patients with a Ki67 index ≥ 5% in cerebral convexity meningiomas was significantly higher than in non-cerebral convexity location. This result corroborates our conclusion that cerebral convexity location

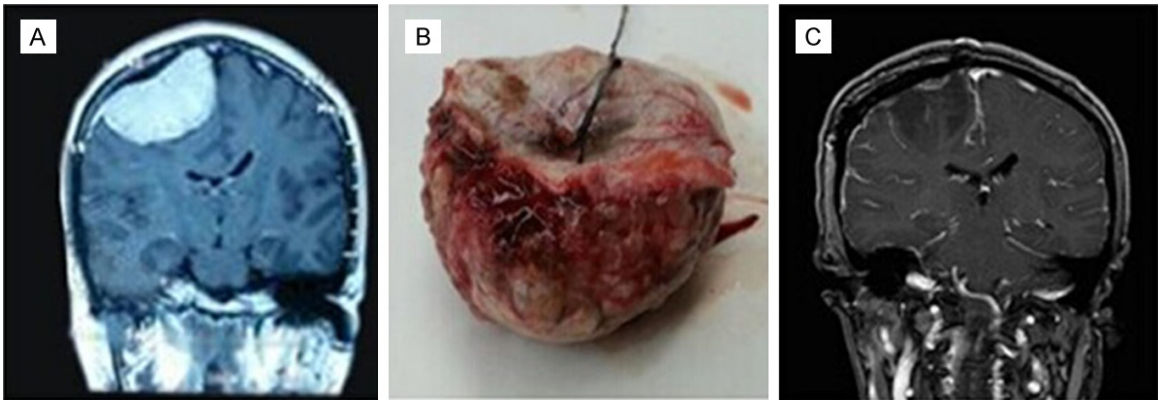

Figure 1. The patient with meningioma underwent Simpson Grade I resection.

is a risk factor for atypical and anaplastic meningiomas. Hasseleid et al. [18] reported that patients with meningiomas underwent Simpson Grade I resection have a lower recurrence rate than those underwent Simpson resection Grades II and III. Therefore, they believe that convexity meningiomas should reach the goal of Simpson Grade I resection. This is in line with our clinical practice (**Figure 1**).

In this large series, we found that cerebral convexity, male gender are preoperative risk factors for atypical and anaplastic meningiomas. Significant differences in the terms of falx/sagittal sinus and intraventricular were not found. However, the limitations of this research should be acknowledged. First, this is only a retrospective study. Second, the possible association between the anatomical locations and the survival time of patients with meningiomas was not performed. Because the duration of follow-up in this study was so short, that it could not be statistically analyzed. This remained to be carried out in future research.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yan-Hui Liu, Department of Neurosurgery, West China Hospital of Sichuan University, Chengdu, P. R. China. E-mail: Yhliu2011@163.com

References

[1] Deltour I, Johansen C, Auvinen A, Feychting M, Klaeboe L, Schüz J. Time trends in brain tumor incidence rates in Denmark, Finland, Norway, and Sweden, 1974-2003. J Natl Cancer Inst 2009; 10: 1721-1724.

[2] Whittle IR, Smith C, Navoo P, Collie D. Meningiomas. Lancet 2004; 363: 1535-1543.

[3] Sherman WJ, Raizer JJ. Medical management of meningiomas. CNS Oncol 2013; 2: 161-170.

[4] Zhou P, Ma W, Yin S, Li Y, Jiang S. Three risk factors for WHO grade II and III meningiomas: A study of 1737 cases from a single center. Neurol India 2013; 61: 40-44.

[5] Kane AJ, Sughrue ME, Rutkowski MJ, Shangari G, Fang S, McDermott MW, Berger MS, Parsa AT. Anatomic location is a risk factor for atypical and malignant meningiomas. Cancer 2011; 117: 1272-1278.

[6] Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, editors. WHO Classification of tumours of the central nervous system. Lyon: IARC Press; 2007.

[7] Bondy M, Ligon BL. Epidemiology and etiology of intracranial meningiomas: a review. J Neurooncol 1996; 29: 197-205.

[8] Rohringer M, Sutherland GR, Louw DF, Sima AA. Incidence and clinicopathological features of meningioma. J Neurosurg 1989; 71: 665-672.

[9] Alvarez F, Roda JM, Perez Romero M, Morales C, Sarmiento MA, Blázquez MG. Malignant and atypical meningiomas: a reappraisal of clinical, histological, and computed tomographic features. Neurosurgery 1987; 205: 688-694.

[10] Cornelius JF, Slotty PJ, Steiger HJ, Hänggi D, Polivka M, George B. Malignant potential of skull base versus non-skull base meningiomas: clinical series of 1,663 cases. Acta Neurochir 2013; 155: 407-413.

[11] Mahmood A, Caccamo DV, Tomecek FJ, Malik GM. Atypical and malignant meningiomas: a clinicopathological review. Neurosurgery 1993; 33: 955-963.

[12] Mahmood A, Qureshi NH, Malik GM. Intracranial meningiomas: analysis of recurrence after

surgical treatment. Acta Neurochir 1994; 126: 53-58.
[13] Marosi C, Hassler M, Roessler K, Reni M, Sant M, Mazza E, Vecht C. Meningioma. Crit Rev Oncol Hematol 2008; 67: 153-171.
[14] Pasquier D, Bijmolt S, Veninga T, Rezvoy N, Villa S, Krengli M, Weber DC, Baumert BG, Canyilmaz E, Yalman D, Szutowicz E, Tzuk-Shina T, Mirimanoff RO; Rare Cancer Network. Atypical and malignant meningioma: outcome and prognostic factors in 119 irradiated patients. A multicenter, retrospective study of the Rare Cancer Network. Int J Radiat Oncol Biol Phys 2008; 71: 1388-1393.
[15] Wang DJ, Xie Q, Gong Y, Mao Y, Wang Y, Cheng HX, Zhong P, Che XM, Jiang CC, Huang FP, Zheng K, Li SQ, Gu YX, Bao WM, Yang BJ, Wu JS, Xie LQ, Zheng MZ, Tang HL, Zhu HD, Chen XC, Zhou LF. Histopathological classification and location of consecutively operated meningiomas at a single institution in China from 2001 to 2010. Chin Med J (Engl) 2013; 126: 488-493.
[16] Jaaskelainen J, Haltia M, Servo A. Atypical and anaplastic meningiomas: radiology, surgery, radiotherapy, and outcome. Surg Neurol 1986; 25: 233-242.
[17] Roser F, Samii M, Ostertag H, Bellinzona M. The Ki-67 proliferation antigen in meningiomas. Experience in 600 cases. Acta Neurochir (Wien) 2004; 146: 37-44.
[18] Hasseleid BF, Meling TR, Ronning P, Scheie D, Helseth E. Surgery for convexity meningioma: Simpson Grade I resection as the goal: clinical article. J Neurosurg 2012; 117: 999-1006.