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Clinical Study

Survival rates, prognostic factors and treatment of anaplastic meningiomas

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ABSTRACT

Intracranial anaplastic meningioma is a malignant type of meningioma with a high rate of recurrence and death. Given its rarity, minimal information regarding this tumour is available. Thus, we studied a series of patients with anaplastic meningiomas and analysed the survival rates, prognostic factors and treatment methods associated with these patients. Forty-three anaplastic meningioma cases treated at our hospital between July 2002 and June 2012 were compiled into a single database used to summarise the clinical characteristics from a retrospective review of patient records. Progression free survival (PFS) and overall survival (OS) were analysed as a function of each possible prognostic factor. The 1, 3 and 5 year PFS rates were 90.7%, 51.3%, and 37.0%, respectively, whereas the corresponding values of OS rates were 95.3%, 68.0% and 49.2%, respectively. A number of factors were selected to analyse association with prognosis. Simpson Grade I and II resections exhibited increased PFS rates and radiotherapy improved the OS rate in anaplastic meningiomas. Tumours with homogeneous contrast enhancement on MRI were associated with increased PFS and OS. Sex, age, tumour location, first or transformed anaplastic tumour, pre-operative Karnofsky Performance Scores, tumour volumes and bone involvement had no significant effect on either PFS or OS. MRI homogeneous contrast may be a useful prognostic factor and surgery followed by radiotherapy is recommended for the treatment of anaplastic meningiomas.

1. Introduction

Meningiomas constitute approximately 20% of all brain tumours [1]. Based on the World Health Organization (WHO) 2007 classification system, meningiomas are classified into three grades, I–III, with 16 different variants or subtypes [2]. Grade III meningiomas exhibit a higher rate of recurrence and death compared with Grade I and II tumours and are associated with increased morbidity and mortality [3,4,6–8]. Grade III meningiomas are anaplastic meningiomas with high mitotic activity ($\geqslant$20/10 high-power fields) and/or obviously malignant cytology. Rare meningioma variants, including papillary and rhabdoid meningiomas, are also categorised as Grade III [9]. Anaplastic meningiomas are the most common type of Grade III meningiomas and account for 1–3% of all meningiomas [3–5]. Given the rarity of this tumour, few papers have reported on the prognosis and treatment of anaplastic meningiomas.

Radical surgical resection is recognised as a prognostic factor in Grade I and II meningiomas [10]. Radiotherapy is not recommended after radical resection of Grade II meningiomas [11]. Tumour heterogeneous contrast enhancement is a radiological factor associated with a higher risk of meningioma recurrence [12]. However, the influence of surgery and radiotherapy on the prognosis of anaplastic meningiomas is still under investigation. Whether heterogeneous contrast enhancement is related to the prognosis of anaplastic meningiomas has not been reported. In this study, we analysed the outcomes and treatment of anaplastic meningiomas and sought to detect factors useful for predicting outcome and improving the management of these tumours.

2. Methods and materials

2.1. Patient and data collection

We retrospectively reviewed our case database and the pathological records from our hospital between July 2002 and June 2012. The pathology reports indicating anaplastic meningioma were used to identify patients included in our study. Transformed anaplastic meningiomas, where the initial operation was performed in our department and the initial diagnosis was benign or atypical meningioma, were also included. Patients who

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underwent their first surgery in other hospitals were excluded. In total, 43 cases of anaplastic meningioma had follow-up data available.

Data regarding the patient's age at operation, sex, symptoms and pre-operative Karnofsky Performance Scores (KPS) were collected. Initial imaging was performed with contrast-enhanced MRI. Data regarding the location of the tumour and characteristics of contrast enhancement were obtained from the imaging. Tumour location was divided into the following six groups: convexity, falx, parasagittal, cranial base, posterior cranial fossa and lateral ventricle trigone area. Contrast-enhanced MRI scans were classified into two groups: homogeneous or heterogeneous contrast enhancement. Surgical resection was graded according to the Simpson Grade and grading was deduced from the operation records and post-operative MRI. The tumour volume was calculated using the following formula: $\pi/6 \times \text{length} \times \text{width} \times \text{height}$. Bone involvement was recorded if it was described in the operation or pathological reports.

The post-treatment MRI examination was performed 3 months after the operation and every 3–6 months annually thereafter. Recurrence was diagnosed if regrowth was detected by follow-up MRI. The use of radiotherapy, recurrence time and length of survival were obtained from outpatient follow-up or telephone interview. Progression free survival (PFS) was defined as the time between tumour treatment and the most recent imaging study demonstrating radiographic tumour absence or progression. All patients were evaluated to confirm the pathological diagnosis and to classify the tumours according to the 2007 WHO classification system. Meningiomas with high mitotic activity ($\geqslant$20/10 high-power fields) were classified as anaplastic.

2.2. Statistical analysis

A descriptive analysis of the population was performed using SPSS Statistics software (version 19.0; IBM Corporation, Armonk, NY, USA). Statistical analysis of overall survival (OS) and PFS was performed by comparing computer generated curves estimated by the Kaplan–Meier method. Differences in OS and PFS curves were assessed using the log-rank test. p values were considered significant at 5% ($p < 0.05$). Cox univariate and multivariate regression analyses were used to assess the correlation between various factors and survival. The factors studied included sex, age, tumour location, first or transformed tumour, pre-operative KPS, homogeneous or heterogeneous contrast enhancement on MRI, operative Simpson Grade, tumour volume, bone involvement and radiotherapy.

3. Results

3.1. Clinical characteristics

Of the 43 anaplastic meningioma patients, there were 27 men and 16 women, with a male to female ratio of 1.69:1. The average age at the time of initial diagnosis was 48.4 years (range, 10–76 years; standard deviation ± 15.1). The presentation included headache (51.2%), neurological deficits (23.3%), epilepsy (13.9%) or asymptomatic (11.6%). The proportion of pre-operative KPS scores $\geqslant$80 and <80 was 46.5% and 53.5%, respectively. All patients underwent a contrast-enhanced MRI before the operation and homogeneous (72.1%) and heterogeneous contrast enhancement (27.9%) were identified. In this study, tumour location was classified into six categories: convexity (25.6%), falx (9.3%), parasagittal (18.6%), cranial base (30.3%), posterior fossa (7.0%) and lateral ventricle trigone (9.3%). The tumour samples, including first operative pathology, were categorised as anaplastic (65.1%) and transformed anaplastic meningiomas (34.9%) (nine patients had benign initial tumours and six patients atypical). Of the 43 patients, 37.2%, 30.2%, 27.9% and 4.7% underwent Simpson Grade I, II, III, and IV resections, respectively. None of the patients were categorised as Simpson Grade V. The median tumour volume was 50 cm^3 (range, 3–216). Bone involvement occurred in 18 of 43 patients (41.9%; Table 1).

3.2. PFS and OS

The mean follow-up period was 44 months (range, 9–122). At the last follow-up, 24 patients (55.8%) presented with a recurrent tumour or tumour regrowth 6–90 months after the operation. The median PFS and OS were 46 months and 59 months, respectively. The 1, 3, and 5 year PFS rates were 90.7%, 51.3%, and 37.0%, respectively (Fig. 1). The 1, 3, and 5 year OS rates were 95.3%, 68.0%, and 49.2%, respectively (Fig. 2).

3.3. Simpson Grades and survival

Because of the limited number of cases and the fact that posterior cranial fossa meningiomas can rarely be completely resected, we combined the Simpson Grade I and II surgeries. The remaining 14 patients underwent Simpson Grade III–IV resection. In total, recurrence occurred in 14 of 29 Simpson Grade I–II (49.3%) and 10 of 14 Simpson Grade III–IV resections (71.4%). The PFS values were compared between Simpson Grade I–II and Simpson Grade III–IV surgeries. For Simpson Grade I–II resections, the 1 and 3 year PFS rates were 89.7% and 64.7%, respectively, and for Simpson Grade III–IV surgeries 57.1% and 23.9%, respectively. The difference was statistically significant based on log-rank analysis ($p = 0.01$;

Table 1
Clinical characteristics of 43 patients with anaplastic meningiomas

Characteristic	Number, n (%)
Sex	
Male	27 (62.8)
Female	16 (37.2)
Mean age (years ± SD)	48.4 ± 15.1
Presentation	
Headache	22 (51.2)
Neurological deficits	10 (23.3)
Epilepsy	6 (13.9)
Asymptomatic	5 (11.6)
Location	
Convexity	11 (25.6)
Falx	4 (9.3)
Parasagittal	8 (18.6)
Cranial base	13 (30.3)
Posterior fossa	3 (7.0)
Lateral ventricle trigone area	4 (9.3)
First or transformed tumor	
First	28 (65.1)
Transformed from benign	9 (20.9)
Transformed from atypical	6 (14.0)
Pre-operative KPS scale	
$\geqslant$80	20 (46.5)
<80	23 (53.5)
Contrast enhancement on MRI	
Homogeneous	31 (72.1)
Heterogeneous	12 (27.9)
Simpson Grade	
I	16 (37.2)
II	13 (30.2)
III	12 (27.9)
IV	2 (4.7)
Tumor volume (cm^3)	50 (range, 3–216)
Bone involvement	18 (41.9)
Radiotherapy	33 (76.6)
Recurrence	24 (55.8)
Death	19 (44.2)

KPS = Karnofsky Performance Score, SD = standard deviation.