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Brief communication: Recurrent brain meningiomas

John J. Guarnaschelli, MD [1], S. P. Stawicki, MD [2]

[1] Neurosurgical Group of Greater Louisville, Louisville, KY, USA

[2] Principal Scientist, OPUS 12 Foundation, King of Prussia, PA, USA

ABSTRACT

Meningiomas constitute the second most common type of central nervous system neoplasm. Overall, these tumors represent approximately 14-30% of all central nervous system neoplasms. Brain meningiomas are usually benign. They arise from the intracranial and spinal meninges and their dural extensions. When grouped according to the WHO classification, approximately 80% of meningiomas are Grade I (benign), with the remaining 20% being either Grade II (atypical) or Grade III (malignant) lesions. The recurrence rate of meningiomas varies from 4% to 50% depending on the tumor grade, completeness of resection, and other clinical, pathologic, and radiographic factors. The authors present their experience with 333 operative cases of brain meningioma treated over a period of 25 years. This brief communication concentrates on the description of the patient subset with recurrent meningiomas.

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Correspondence to: S. P. Stawicki, MD. OPUS 12 Foundation, 304 Monroe Blvd, King or Prussia, PA, 19406 USA.

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Meningiomas are the second most common type of central nervous system neoplasm, accounting for approximately 14-30% of all central nervous system tumors.[1-3] Brain meningiomas are mostly benign neoplasms. They arise from the intracranial and spinal meninges and their dural extensions.[2] When grouped according to the WHO classification, approximately 80% of meningiomas are Grade I (benign), with the remaining 20% being either Grade II (atypical) or Grade III (malignant) (**Table 1**).[2,4-5] The recurrence rate of meningiomas varies between 4% and 50% depending on the tumor grade, completeness of resection, among other factors.[4,6] The authors present their experience with 333 operative cases of brain meningioma treated over a period of 25 years. This brief communication concentrates on the patient subset with recurrent meningiomas.

Table 1. Pathologic grading of meningiomas based on the WHO classification.[5]

Grade	Designation	Meningioma characteristics
I	Typical	Meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, clear cell, choroid, lympho-plasmacyte-rich, metaplastic
II	Atypical	Papillary
III	Anaplastic	Malignant

Brain meningiomas account for approximately 13% of all brain neoplasms in our institutional database of 2500 patients with brain tumors. In terms of demographics, female patients outnumbered males in the overall sample (**Table 2**, P<0.001). Most patients presented between the ages of 40 and 60 years, with a mean age of 56 years. Presenting symptoms were typical of brain tumors in general, resulting from either mass effect, focal signs, or both. Headache was the most common presenting symptom (24%), followed by visual deficit (13%), seizures (9.6%), and cognitive deficits (6.9%). The most common anatomic locations of meningiomas in this study were convexity (15.4%) followed by frontal (11.2%) and parasagittal (10.9%) regions (**Table 2**). This overall distribution of lesions is in good agreement with previously published data.[5-9]

Table 2. Basic characteristics of the overall meningioma sample and the subset of patients with recurrent meningiomas.

All meningioma patients			
	Gender	M 90 (27%)	F 243 (73%)
	Age (years)	<40 (n = 48, 14.4%)	
		40-60 (n = 154, 46.2%)	
		>60 (n = 131, 39.3%)	
		Mean age 56 ± 14, range 11 to 87 years	
	Location	Convexity (15.4%); Frontal (11.2%); Parasagittal (10.9%); Sphenoid ridge (7.9%); CPA (7.5%); Tuberculum sellae (6.1%); Olfactory groove (4.8%); Posterior fossa (4.1%); Occipital (3.8%)	
	Histology	Benign (72%); Intermediate to high grade (9.3%); Fibroblastic (7.9%); Transitional (6.2%); Psammomatous (3.8%); Mixed type (3.3%)	
Recurrences			
	Gender	M 14 (45.2%)	F 17 (54.8%)
		16% of all males	7% of all females
	Time to recurrence	Mean of 84 months, range 12-240 months	
	Age	<40 (n = 9, 29%)	
		40-60 (n = 17, 55%)	
		>60 (n = 5, 16%)	
		Range 11 to 72 years	
	Location	Convexity (25.8%); CPA (12.9%); Middle fossa (12.9%); Olfactory groove (9.7%); Posterior fossa (6.5%)	
	Histology	Meningotheliomatous (38.7%); Benign (22.6%); Transitional (9.7%); Fibroblastic (9.7%); Malignant type (6.5%); Syncytial (6.5%); Angioblastic (3.2%)	
	Mortality	3/31 (9.7%)	
		75% of total meningioma mortalities	

All patients in this series underwent advanced brain imaging (computed tomography – CT or magnetic resonance imaging - MRI) prior to operative intervention. Following surgical tumor removal, all patients had their diagnosis confirmed by light microscopy (LM) and 38% of tumors underwent additional diagnostic confirmation by electron microscopy (EM). Most of the tumors in this series were benign (**Table 2**). This is consistent

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with the generally described characteristics of meningiomas as being mostly benign in nature.[2,6] In fact, even with higher-grade tumors most recurrences tend to be local, and only approximately 0.1% of meningiomas are known to metastasize.[2,7]

Out of the total 333 patients in this series, 31 (9.3%) had a documented recurrent meningioma as demonstrated by computed tomography (CT) and/or magnetic resonance imaging (MRI) of the brain. The mean recurrence time was 84 months (range 12 to 240 months). Patient age ranged from 11 to 72 years in the recurrent group, with male patients being significantly more likely to present with a recurrence than female patients (**Table 2**, $P<0.030$). Mortality among patients with tumor recurrence was 3/31 (9.7%), which accounts for 75% of all meningioma mortalities in this study.

Factors previously cited as being associated with meningioma recurrences include: (a) incomplete surgical resection – see Simpson classification – **Table 3**; (b) atypical and malignant histologic types – see WHO classification – **Table 1**; (c) heterogenous tumor contrast enhancement on CT scan; (d) presence of nucleolar prominence on microscopy; and (e) presence of two or more mitoses per 10 high-power fields on microscopy.[5-6,8] Patients without any of these clinical, radiographic, or pathologic features have low recurrence rates (approximately 4% at 5 years and 18% at 10 years).[6,9]

Table 3. Resection-based grading of meningiomas, derived from the Simpson classification.[8]

Grade	Recurrence	Tumor resection
I	9%	Macroscopically complete removal, includes dura and bone
II	***19%***	***Macroscopically complete removal, dural coagulation***
III	29%	Complete removal, dura not coagulated
IV	***44%***	***Partial tumor removal***
V	---	Simple decompression

All thirty-one patients (9.3% of the entire meningioma sample) required surgical intervention for their recurrence. A total of 19 patients in the recurrent group had both light microscopy (LM) and electron microscopy (EM) performed. For these 19 patients, the sites of recurrence, from most frequent to least frequent, were: (a) convexity 8/19; (b) cerebellopontine angle - CPA 4/19; (c) cavernous sinus 3/19; (d) sagittal sinus-falx 2/19; (e) olfactory groove 1/19; and (f) tuberculum 1/19. **Table 4** shows meningioma recurrence rates in major published series.

Electron microscopy, when compared to routine LM, radiographic appearance of invasiveness, and the degree of surgical resection, did not appear to provide any additional value in predicting tumor recurrence. In fact, EM showed the tumor to be more aggressive than LM in only one patient (cavernous sinus meningioma). The relative lack of predictive value based on traditional meningioma classifications prompted an ongoing search for alternative means of forecasting the biologic behavior of these tumors based on modern molecular biology techniques.[4] For example, there is some data to suggest that molecular signatures could help distinguish slower-growing atypical meningiomas from more aggressive ones.[4] Moreover, analyses of genomic alterations in benign, atypical, and anaplastic meningiomas may ultimately help clinicians predict the natural behavior of these tumors based on individualized, patient- and tumor-specific characteristics (**Figure 1**).[7]

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Table 4. Meningioma recurrence rates in major published series.

Study (Reference)	Number of patients	Recurrence rate
Adegbite (10)	114	20%
Cushing-Eisenhardt (11)	313	33%
Jaas-Kelainen (12)	159	19%
Marks (13)	53	20%
Miller (14)	105	26%
Mirimanoff (15)	225	32%
Stafford (16)	581	25%
Current series	333	9.3%

The overall mortality among recurrent meningiomas in this series was 9.7%, and recurrence-related mortality constituted 75% of all meningioma-related mortality. Traditionally, reported survival rates associated with brain meningiomas are over 80% at two years, 70% at 5 years, and 60% at 10 years.[6] The survival rate in the current series is slightly higher than that reported in most major series. In terms of morbidity, it is well established that neurologic complications among patients who underwent meningioma resection are significantly more common in patients with advanced age. In fact, among patients older than 70 years who underwent surgery for meningioma, the neurologic complication rate is over 20% while it is less than 5% in younger patients.[6] In addition, postoperative results tend to be better in patients with fewer co-morbid conditions, smaller meningiomas, less associated edema, shorter surgery times, and a more accessible tumor location (i.e., convexity rather than skull base).[6]

CONCLUSIONS

In summary, recurrent meningiomas are relatively common, constituting 9.3% of cases in this study. While female patients were more likely to present with a meningioma, male patients were more likely to have a recurrence. The overall mortality among recurrent meningiomas was 9.7%, and recurrence-related mortality constituted 75% of all meningioma-related mortality in this series. The ability to perform total versus subtotal removal of the tumor was a good predictor of recurrence, with most of the recurrences occurring in the subtotal resection group and only a few occurring in patients who underwent total removal. Other variables that appeared to be useful in predicting tumor recurrence included tumor size, radiographic appearance of the tumor, invasion of the skull base, and histologic appearance on light microscopy. Electron microscopy did not appear to offer any additional prognostic advantage.

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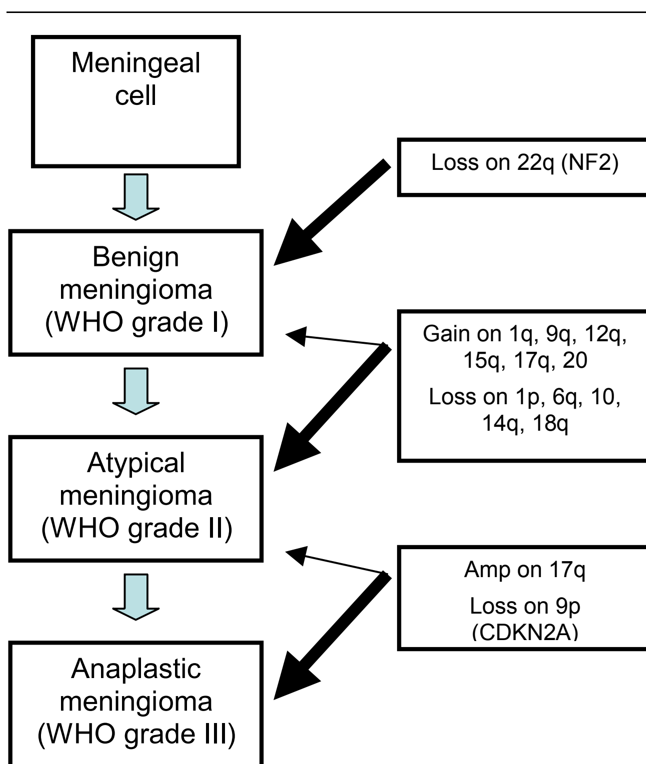

Figure 1. Model of genomic alterations involved in pathologic progression of brain meningioma. Abnormalities are listed according to tumor grade in which they were first detected at a frequency of more than 30%. However, the changes may already have occurred in lower grade lesions in a small percentage of patients (illustrated by thin arrows). Modified from Weber RG, Bostrom J, Wolter M, Baudis M, Collins VP, Reifenberger G, Lichter P. Analysis of genomic alterations in benign, atypical, and anaplastic meningiomas: Toward a genetic model of meningioma progression. Proc Natl Acad Sci U S A 1997;94:14719-14724.

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