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Risk factors for malignant and atypical meningiomas

Abstract

Objective: In this study a large series of our patients have been reviewed to determine risk factors for atypical and malignant meningioma, with particular interest paid to previous surgeries, tumor location, patient's age and gender.

Methods: The authors reviewed the records of 420patients who underwent surgery at King Hussein Medical Center between 2003 to 2015 with histologically confirmed meningioma, the age of the patient is the age at time of surgery, pathology grading according to the World Health Organization 2007 guidelines, and tumor location confirmed with preoperative imaging and operative notes.

Results: Risk factors for atypical and malignant meningioma included patients with previous surgery had three times increase incidence of atypical or malignant meningiomas, non skull base location and male sex doubled the risk, but the patient's age had no any significance as risk factor.

Conclusion: Previous surgery, male sex and non skull-base meningiomas increased the risk for malignant and atypical meningiomas. This increased possibility of recurrence after surgical resection and patients need for radiotherapy (conventional or stereotactic). So, it is important to take these factors regarding the patient's plan of management and prognosis.

Keywords: meningioma, malignant, atypical, world health organization grade, surgery

Volume 3 Issue 1 - 2016

Amer Al-Shurbaji, Ra'ed Al-Jubour
Department of Neurosurgery, King Hussein Medical Center (KHMC), Jordan

Correspondence: Ra'ed Al-Jubour, Neurosurgery department, King Hussein Medical Center, (KHMC), Amman-Jordan, Email readmj@yahoo.com

Received: January 25, 2016 | **Published:** March 21, 2016

Introduction

In 1922, Harvey Cushing wrote: There is nothing today in the whole realm of surgery more gratifying than the successful removal of a meningioma with subsequent perfect functional recovery; especially should a correct pathological diagnosis have been previously made. The difficulties are admittedly great, sometimes insurmountable, and though the disappointments still are many, another generation of neurological surgeons will unquestionably see them largely overcome.[1] Ninety years later Cushing's prophecy is very much fulfilled. Due to advances in neuroimaging the preoperative diagnosis of a meningioma is almost certain. Indeed, the successful removal of meningiomas with perfect functional recovery has been achieved in most of cases. The dilemma, however, remains with those meningiomas that misbehave those tend to recur and have an aggressive course, or defy the available means of treatment.

Meningiomas are the most common extra-axial primary brain tumor,[2] they occur at a rate of about 2 in 100,000,[3] and in one large surgical series, they accounted for approximately 20% of the brain tumors.[4] Grade II (atypical) and grade III (malignant) meningiomas have higher rates of tumor recurrence than grade I meningiomas after surgery and/or external irradiation. It is becoming increasingly important to assess the likelihood that a tumor is not benign before treatment initiation, although a majority of meningiomas are low grade, a significant proportion will recur after initial treatment. 2 Literature published since the World Health Organization (WHO) 2000 classification reports higher recurrence rates at 5years after surgical excision for WHO grade II (41%)[5,6] and III (70%-91%)[6,7] than for WHO grade I lesions (3%).[6] This study focus in the risk factors for these malignant and atypical meningiomas, and went to be sure that if tumor location, patients age, previous surgeries and gender are significant risk factor.

Methods

This study was approved by the ethical committee on the human research at the Royal Medical services. World Health Organization (WHO) 2007 classification is used as the standard histopathological classification for this retrospective study. Four hundred twenty patients undergoing neurosurgical intervention at the King Hussein Medical Center are prospectively enrolled in a database; we identified all patients between 2003 and 2015 who underwent evaluation and treatment for meningioma at our institution. This research excluded all patients with neurofibromatosis type 2 and all patients with any other intracranial tumor history, also spinal meningiomas were excluded from this study.

Clinical information was retrospectively collected using patient medical records, radiological data, and histopathological reports from both Al-Hussein Hospital records and Princess Salma Laboratory and research center records. All pre and post operative assessments were performed by a neurosurgeon. Patient age was defined by age at the time of surgery. The preoperative, post contrast T1 magnetic resonance images (MRI) and operative notes were reviewed to confirm tumor location (skull base v/s non skull base). A wide variety of meningioma locations were represented in (Table 1). Risk factors for atypical and malignant meningiomas were selected for analysis based on a priori hypotheses from previously published literature.[8–11]

Table 1 Meningioma distribution by WHO grading and anatomical location

Location	Grad 1	Grad 2	Grad 3	Total No.
Clinoid*	3	0	0	3
Clivus*	2	0	0	2
CPA*	13	1	0	14
Convexity**	73	16	4	93
Falx**	26	7	2	35
Foramen magnum*	8	0	0	8
Intraventricular**	5	2	0	7
Jugular foramen*	2	0	0	2
Middle fossa*	15	2	0	17
Multifocal**	16	2	1	19
Olfactory groove*	12	4	0	16
Parasagittal**	59	14	4	77
Parasellar*	22	3	0	25
Petroclival*	7	0	0	7
Petrous*	9	1	0	10
Posterior fossa*	17	2	0	19
Sphenoid wing*	29	9	0	38
Tentorium*	8	0	0	8
Tuberculum*	18	2	0	20
Total No.	344	65	11	420
Percentage	82%	15.5%	2.5%	100%

*Skull base meningiomas, **Non skull base meningiomas.

WHO, world health organization; CPA, cerebellopontine angle

Results

Between 2003 to 2015 four hundred twenty patients underwent craniotomy for removal of a histologically proven meningioma, 295patients were females 70%, 125patients were males 30%. The age range was 18 to 87years and the mean age was 51years. The frequencies of WHO grade I were 82%(344patients), grad II 15.5%(65 patients) and grad III 2.5%(11patients). Convexity meningiomas less than three cm. are frequently observed, and surgical intervention may only occur for large tumors (>3cm), interval growth, symptom development, or radiographic findings indicating aggressive disease course. We found <5% of patients with a convexity meningioma underwent surgery for interval growth or atypical MRI features, whereas >95% of these patients underwent surgery because of tumor size>3 cm or for significant clinically debilitating symptoms.

Previous surgery for tumor excision was also found to be strongly associated with increased risk for high-grade pathology on univariate analysis (54% v/s 18%, P>0.001), which increase the risk for high grad meningioma three times. Non skull base meningioma is significant risk factor and doubles the risk for atypical and malignant meningiomas (31% v/s 11%, P>0.001) (Table 2). Although 70% of the patients were female, we found that a disproportionate number of males had higher-grade pathology on univariate analysis (32% v/s 15%, P>0.001). On univariate analysis there was a trend for patients older than 65years to have increased risk of malignant or atypical meningiomas (26% v/s 18%, P=0.13). We therefore included age >65years as a covariate in our multivariate regression; however, it was not found to be a significant risk factor for atypical or malignant pathology.

Table 2 Univariate analysis for potential risk factor in patients with grad II and III WHO meningiomas

Characteristic	Frequency	%	*P*
Previous surgeries	18	54%	<0.001
No previous surgeries	58	18%	
Skull base	25	11%	<0.001
Nonskull base	51	31%	
Male	31	32%	<0.001
Female	45	15%	
Age <65years	52	18%	0.13
Age >65years	24	26%	

WHO, world health organization

Discussion

Surgical resection was the standard treatment for meningiomas since 1887, W.W. Keen described the first successful removal of a meningioma in the United States.[12] Nowadays the degree of surgical resection is the most important factor for recurrence especially for classical meningiomas, Simpson classified is clinical classification for meningioma resection as follows: Grade one, complete removal, including resection of dura and bone; Grade two, complete tumor removal with coagulation of dural attachment; Grade three, complete tumor removal without resection or coagulation of dural attachments; Grade four, subtotal removal; and Grade five, decompression. This classification is very useful for evaluating recurrences rates, as we go from Grade I through Grade IV tumors the recurrence rates increase 9%, 19%, 29%, and 40%, respectively; at 10years follow up.[13] Risk factors (tumor location, previous surgeries and gender) that can predict meningioma grade before tissue diagnosis will guide surgeons toward optimal treatment by helping to balance the risk of surgical morbidity with the need for tissue diagnosis.[14–20]

This study confirmed that patients who had undergone prior surgery were more likely to have a non skull base meningioma, and had three times increased risk for malignant or atypical meningiomas at the time of second surgery. Benign meningiomas have a high level of progesterone receptor expression relative to atypical and malignant meningiomas. Clinical and histopathologic studies have shown an inverse relationship between progesterone receptor expression level and both WHO grade and recurrence.[21–23] Risk for atypical and malignant changes increased with non skull base meningiomas. Sade and colleagues[10] found a larger risk reduction for skull base meningiomas four times compared with our study which double the risk; the mechanism underlying this risk difference may result from the distinct embryologic origin of skull base and non skull base dura.[10,24,25]

Increase rates of atypical and malignancy among the convexity and parasagittal and the relatively poor tumor control rates published for malignant or atypical meningiomas treated with stereotactic radiotherapy.[5,7,26–28] Also, our data analysis found that male sex double risk for a patient to have an atypical or malignant meningioma. There have been various reports in the literature regarding the association of meningioma grade and anatomical location.[8–11] The mechanism by which male sex increases risk is currently unclear.[29] However, some insight into the biology of this difference can be gained from the scientific literature, which points toward differences in sex chromosome genetic variation, hormone levels and hormone receptor status. Although females have an overall increased incidence of meningiomas, other studies have also reported an increased risk for atypical and malignant meningiomas associated with male sex.[30,31]

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

References

1. Cushing H. The meningiomas (dural endotheliomas): Their source, and favored seats of origin. *Brain*. 1922;45(2):282–306.
2. Louis DN, Ohgaki H, Wiestler OD, et al. *WHO Classification of tumours of the central nervous system*. Lyon, France: IARC Press; 2007. 312 p.
3. Rohringer M, Sutherland GR, Louw DF, et al. Incidence and clinicopathological features of meningiomas. *J Neurosurg*. 1989;71(5 Pt 1):665–672.
4. Rachlin JR, Rosenblum ML. Etiology and biology of meningiomas. In: Al-Mefty O editor. *Meningiomas*. Raven, New York, USA; pp. 22-37.
5. Aghi MK, Carter BS, Cosgrove GR, et al. Long-term recurrence rates of atypical meningiomas after gross total resection with or without postoperative adjuvant radiation. *Neurosurgery*. 2009;64(1):56–60.
6. Nakasu S, Fukami T, Jito J, et al. Recurrence and regrowth of benign meningiomas. *Brain Tumor Pathol*. 2009;26(2):69–72.
7. Yang SY, Park CK, Park SH, et al. Atypical and anaplastic meningiomas: prognostic implications of clinicopathological features. *J Neurol Neurosurg Psychiatry*. 2008;79(5):574–580.
8. Sade B, Chahlavi A, Krishnaney A, et al. World Health Organization grades II and III meningiomas are rare in the cranial base and spine. *Neurosurgery*. 2007;61(6):1194–1198.
9. Mahmood A, Caccamo DV, Tomecek FJ, et al. Atypical and malignant meningiomas: a clinicopathological review. *Neurosurgery*. 1993;33(6):955–963.
10. Maier H, Ofner D, Hittmair A, et al. Classic, atypical, and anaplastic meningioma: 3 histopathological subtypes of clinical relevance. *J Neurosurg*. 1992;77(4):616–623.
11. Liu Y, Liu M, Li F, et al. Malignant meningiomas: a retrospective study of 22cases. *Bull Cancer*. 2007;94(10):E27–31.
12. Bingham WF. WW Keen and the dawn of American neurosurgery. *J Neurosurg*. 1986;64(5):705–712.
13. Simpson D. Recurrence of intracranial meningiomas after surgical treatment. *J Neurol Neurosurg Psychiatry*. 1957;20(1):22–39.
14. Flickinger JC, Kondziolka D, Maitz AH, et al. Gamma knife radiosurgery of imaging-diagnosed intracranial meningioma. *Int J Radiat Oncol Biol Phys*. 2003;56(3):801–806.
15. Kondziolka D, Mathieu D, Lunsford LD, et al. Radiosurgery as definitive management of intracranial meningiomas. *Neurosurgery*. 2008;62(1):53–58.
16. Herscovici Z, Rappaport Z, Sulkes J, et al. Natural history of conservatively treated meningiomas. *Neurology*. 2004;63(6):1133–1134.
17. Bindal R, Goodman JM, Kawasaki A, et al. The natural history of untreated skull base meningiomas. *Surg Neurol*. 2003;59(2):87–92.
18. Braunstein JB, Vick NA. Meningiomas: the decision not to operate. *Neurology*. 1997;48(5):1459–1462.
19. Olivero WC, Lister JR, Elwood PW. The natural history and growth rate of asymptomatic meningiomas: a review of 60 patients. *J Neurosurg*. 1995;83(2):222–224.
20. Nakamura M, Roser F, Michel J, et al. The natural history of incidental meningiomas. *Neurosurgery*. 2003;53(1):62–70.
21. Korhonen K, Salminen T, Raitanen J, et al. Female predominance in meningiomas cannot be explained by differences in progesterone, estrogen, or androgen receptor expression. *J Neurooncol*. 2006;80(1):1–7.
22. Whittle IR, Foo MS, Besser M, et al. Progesterone and oestrogen receptors in meningiomas: biochemical and clinicopathological considerations. *Aust N Z J Surg*. 1984;54(4):325–330.

23. Wolfsberger S, Doostkam S, Boecher-Schwarz HG, et al. Progesterone-receptor index in meningiomas: correlation with clinico-pathological parameters and review of the literature. *Neurosurg Rev*. 2004;27(4):238–245.

24. Lee JH, Sade B, Choi E, et al. Meningothelioma as the predominant histological subtype of midline skull base and spinal meningioma. *J Neurosurg*. 2006;105(1):60–64.

25. Kepes JJ. Presidential address: the histopathology of meningiomas. A reflection of origins and expected behavior? *J Neuropathol Exp Neurol*. 1986;45(2):95–107.

26. Sughrue ME, Sanai N, Shangari G, et al. Outcome and survival following primary and repeat surgery for world health organization grade III meningiomas. *J Neurosurg*. 2010;113(2):202–209.

27. Durand A, Labrousse F, Jouvet A, et al. WHO grade II and III meningiomas: a study of prognostic factors. *J Neurooncol*. 2009;95(3):367–375.

28. Jaaskelainen J, Haltia M, Servo A. Atypical and anaplastic meningiomas: radiology, surgery, radiotherapy, and outcome. *Surg Neurol*. 1986;25(3):233–242.

29. Tabernero MD, Espinosa AB, Maillo A, et al. Patient gender is associated with distinct patterns of chromosomal abnormalities and sex chromosome linked gene-expression profiles in meningiomas. *Oncologist*. 2007;12(10):1225–1236.

30. Rohringer M, Sutherland GR, Louw DF, et al. Incidence and clinicopathological features of meningioma. *J Neurosurg*. 1989;71(5 pt 1):665–672.

31. Kane A, Sughrue E, Rutkowski M, et al. Anatomic location is a risk factor for atypical and malignant meningiomas. *Cancer*. 2011;117(6):1272–1278.