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 420 patients 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

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. 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; they occur at a rate of about 2 in 100,000, and in one large surgical series, they accounted for approximately 20% of the brain tumors. 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

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.
### 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, 295 patients were females 70%, 125 patients were males 30%. The age range was 18 to 87 years and the mean age was 51 years. The frequencies of WHO grade I were 82%(344 patients), grad II 15.5%(65 patients) and grad III 2.5%(11 patients). Convexity meningiomas less than three cm. are frequently observed, and surgical intervention may only occur for large tumors (>3 cm), 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 grade 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 65 years to have increased risk of malignant or atypical meningiomas (26% v/s 18%, P=0.13). We therefore included age >65 years 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 |
| Non-skull base            | 51        | 31%  |        |
| Male                      | 31        | 32%  | <0.001 |
| Female                    | 45        | 15%  |        |
| Age <65 years             | 52        | 18%  | 0.13   |
| Age >65 years             | 24        | 26%  |        |

**WHO, world health organization**

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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 10 years 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.11–15 Risk for atypical and malignant changes increased with non skull base meningiomas. Sade and colleagues10 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.12,26–28 Also, our data analysis found that male sex double increases the risk for meningioma and malignancy. Simpson classified meningiomas into five grades 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 10 years 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

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Conflict of interest

The author declares no conflict of interest.

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