It's Not Your "Run of the Mill" Meningioma: Characteristics Differentiating Low-Grade From High-Grade Meningeal Tumors

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ABSTRACT

Approximately 30% of primary brain tumors are meningiomas; 90% of these are benign. The remaining 10% have aggressive pathological features and significantly higher recurrence rates. Treatments include surgery, radiation therapy, and other medical therapies. Management of these patients involves vigilant neuroradiological imaging, follow-up visits, symptom management, and ongoing patient and family teaching. Even with aggressive treatment modalities, morbidity and mortality rates remain high.

As with other brain tumors, patients with meningiomas present in a number of ways. The tumor may be found incidentally (e.g., during imaging after a motor vehicle accident), when the patient presents with generalized symptoms such as headache or seizure, or after the development of a focal neurological sign such as extremity weakness or visual compromise. When a patient with an extradural, vividly enhancing brain lesion on magnetic resonance imaging (MRI) is first seen by the neurosurgeon, it is often difficult to differentiate a low-grade from a high-grade meningioma. However, if a more aggressive lesion is suspected, patient teaching and perioperative care are different from that provided to a patient with a low-grade, curable meningioma. This article reviews the pathological features of meningiomas, describes the prognostic indicators, discusses management of the patient with the aggressive form, and identifies nursing care considerations in caring for patients with these aggressive tumors.

Incidence and Etiology

Meningiomas are the second most common primary brain tumor reported in the United States each year and account for approximately 30% of primary neoplasms (Central Brain Tumor Registry of the United States, 2004–2005). They develop from the meninges which surround the brain and spinal cord. It is hypothesized that these dural-based tumors actually arise from the arachnoid layer (Burger & Scheithauer, 2007; Hancq, Salmon, Brotchi, & Al, 2004). The peak incidence occurs in the 40- to 70-year-old age group. Meningiomas are rare in children (1.5%) and occur twice as often in women as they do in men (Whittle, Smith, Navoo, & Collie, 2004).

The most recent World Health Organization classification system divides meningeal lesion into three grades. Frequency of occurrence for each grade is outlined in Table 1 (Bruna et al., 2003; Perry, Stafford, & Scheithauer, 1997; Sandhyamani, Rao, Nair, & Radhakrishnan, 2000; Willis et al., 2005).

It is unclear which factors predispose a patient to develop a meningioma. Studies have shown that there is a connection between patients having received previous radiation and subsequent tumor development (e.g., patients having received radiation for head and neck tumors and patients having received low dose radiation for tinea capitis; Gosztonyi, Slowik, & Pasztor, 2004). However, this relationship has not been supported in studies of medical diagnostic x-rays or occupational exposure (Phillips et al., 2005). In addition, patients with neurofibromatosis type 2 are more likely to develop meningiomas (Whittle et al., 2004). Other factors that have been explored as possible risk factors for meningioma development are previous head trauma, previous breast cancer, and elevated estrogen levels. Although case studies and retrospective analysis studies have taken place, to date, there are no definitive data to support these theories (Custer, Koepsell, & Mueller, 2002; Haddad, Al-Mefty, & Abdulrauf,

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TABLE 1. World Health Organization Grading of Meningiomas

Grade	Name	Frequency (%)	Mitotic Rate (Per 10 High-Power Field)	Pathological Features	Subtypes
I	Benign	78–90	<4	Well circumscribed	–
II	Atypical	15–20	≥ 4 < 20	Three of five Loss of lobularity Small cells Prominent nucleoli Increased cellularity Necrosis	Choroids or clear cell
III	Anaplastic	1.6–4	>20	Anaplasia and Brain invasion	Rhabdoid or papillary

2004; Phillips et al., 2002; Shaw, Kissun, Boyle, & Triantafyllou, 2004).

Imaging Characteristics

Meningiomas have distinct radiographic features. On MRI, they generally appear spherical or globular and homogeneously enhance with the intravenous contrast material. One often sees the characteristic ''dural tail.'' Bone invasion or hyperostosis may also be evident (Fig 1; Akutsu, Sugita, Sonobe, & Matsumura, 2003). Table 2 outlines the most common intracranial locations (Zeltzer, 2004).

Pathological Features

Prognosis after surgery is influenced by age, tumor location, surgical result, and most importantly, pathological features. Tumors that invade brain tissue, have increased mitotic activity, and/or have high proliferation rates are more likely to recur. A mitotic rate of ≥4 per 10 high-power fields (HPF) and at least three of the following pathological features, loss of lobularity, small cells, prominent nucleoli, increased cellularity, and necrosis, are characteristic of aggressive behavior (Perry et al., 1997). A low proliferation rate (Ki-67) of <1% has been associated with favorable progression-free survival (PFS), and a higher proliferation rate of >5% has been associated with a short PFS (Takahashi, Ueba, & Hasimoto, 2004).

Grade I meningiomas are well circumscribed, have low mitotic rates, and have low proliferation rates. Grade II (atypical) meningiomas have ≥4 but less than 20 mitoses per 10 HPF or at least three of the five pathologically aggressive features listed earlier, or are of the choroid or clear cell subtypes, as identified by the pathologist. Grade III (anaplastic) meningiomas are characterized by anaplasia, brain invasion, and ≥20 mitoses per 10 HPF or are of the rhabdoid or papillary subtypes (Perry et al., 1999). Infrequently,

FIGURE 1 Hyperstosis

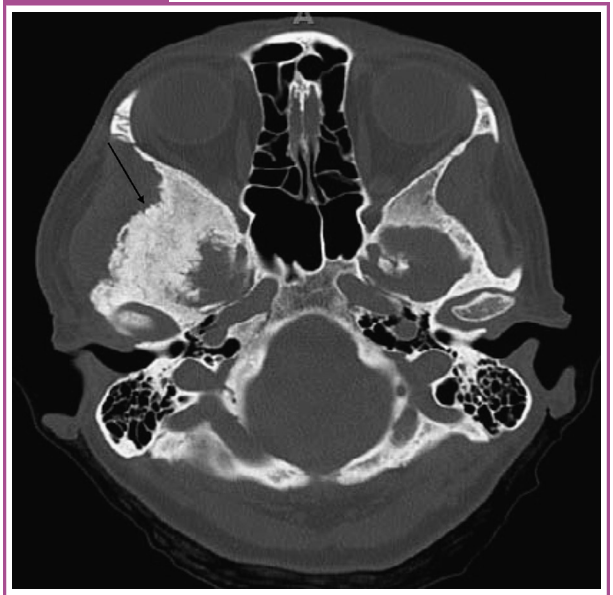


TABLE 2. Meningioma: Common Locations

Location	%
Falx/Parasagittal	25
Convexity	20
Sphenoid wing	18
Olfactory groove	7
Suprasellar	8
Posterior fossa	10
Optic sheath	5
Intraventricular	2
Other brain and spine	5

meningiomas of all grades metastasize within the central nervous system and extracranially. The most common sites of metastasis are lung, liver, and bone (Burger & Scheithauer, 2007; Figueroa, Quint, McKeever, & Chandler, 1999). Figure 2 shows the radiographic differences between the three meningioma grades.

Surgical Management

Tumors consistent with a benign-appearing meningioma on radiographic evaluation are often followed with serial imaging. Surgical intervention is recommended when the tumor is causing symptoms, when it has significant surrounding edema, or when growth is documented over intervening imaging studies. Tumor location limits the extent of surgical resection and increases the risk of recurrence. Tumors located at the sphenoid wing or dural sinuses are more likely to recur. Convexity and suprasellar meningiomas are least likely to recur, given their location and surgical accessibility (Haddad et al., 2004)

The goal of surgery is to attempt a gross total resection, offering the possibility of a cure for low-grade meningiomas. Tumors that involve the bone require craniectomy and cranioplasty to minimize the possibility of recurrence. Postsurgical management includes imaging (MRI) to evaluate the extent of resection and to serve as the new baseline. This patient population is a heterogeneous group, and frequency of radiographic follow-up is case dependent (i.e., location, grade, and extent of resection). Higher grade meningiomas may require further treatment.

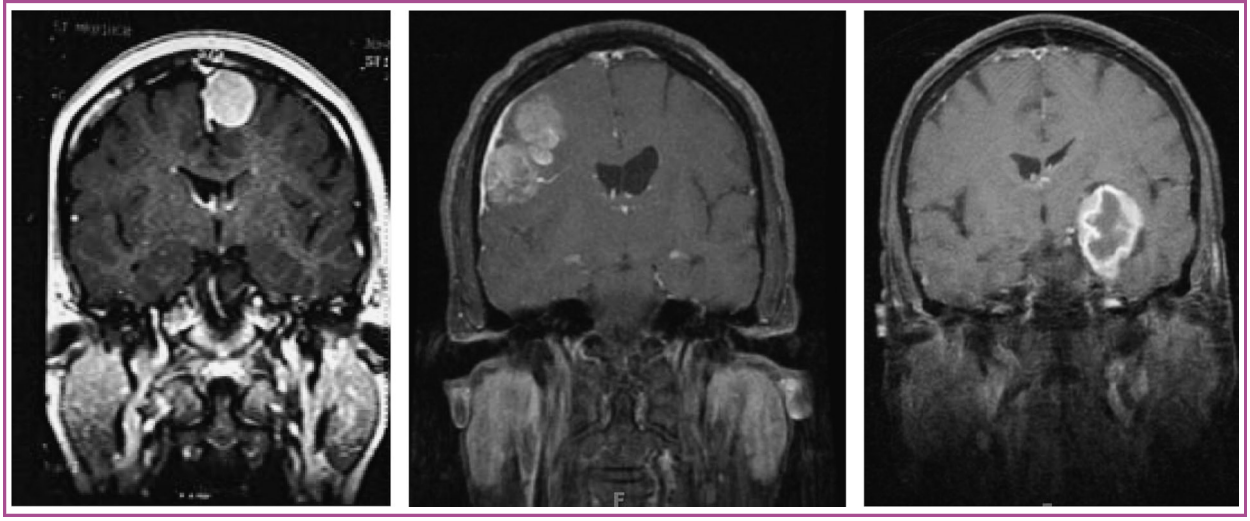
Radiation Therapy

For grade II and III meningiomas, a radiation consult is recommended. The radiation oncologist discusses options for postoperative radiation therapy (RT) with the patient and family to establish both the need and time frame for treatment. Patients with a diagnosis of grade II meningioma who have undergone extensive surgical debulking or gross total resection are frequently advised to obtain serial MRIs to observe for tumor growth. If there is significant residual tumor postoperatively, RT may be recommended. Patients with a diagnosis of grade III are advised to proceed with radiation treatment, even if the postoperative MRI shows little or no obvious residual tumor. The aggressiveness of the tumor warrants an equally aggressive approach to therapy.

Surgical intervention is recommended when a tumor causes symptoms, when surrounding edema exists, or when there is evidence of ongoing tumor growth.

External beam radiation is administered in divided doses (fractions) to residual tumor and surrounding brain tissue, which most likely harbors tumor cells. Fractions allow normal brain tissue to repair during treatment. Doses between 5,400 and 6,000 cGy are recommended. Treatment is performed 5 days a week for approximately 6 weeks. In some cases, a precise form of radiation is administered as a single fraction of high-dose radiation. This is stereotactic radiosurgery. The decision regarding

FIGURE 2 Grades I, II, and III Meningiomas



which form is most appropriate depends on tumor size and location and is made by the radiation oncologist (Pasquier et al., 2007; Rosenberg et al., 2007).

One study looked at PFS after RT in patients having grade II and grade III meningiomas. For patients with grade II lesions, 5-year PFS was 51% and 10-year PFS was 27%. However, the results for grade III meningiomas were less encouraging, with 28% of patients having 5-year and 0% of patients having 10-year PFS. Overall survival was 86% at 5 and 10 years for patients with grade II meningiomas, with 69% survival at 5 years and 45% survival at 10 years in patients with grade III meningiomas (Schulz-Ertner, Milker-Zabel, Thilmann, & Debus, 2005).

Medical Therapies

Medical therapies have also been used against meningiomas that are refractory to surgery and RT. Studies using hydroxyurea, an RNA inhibitor; mifepristone (RU486), a progesterone receptor antagonist; alpha-interferon, a cytokine; and tamoxifen, an estrogen receptor modulator, have shown only modest results and are currently used only in selected cases for atypical and anaplastic meningiomas (Newton, 2007; Wen & Drappatz, 2006). There has also been limited use of chemotherapeutic agents such as cyclophosphamide/doxorubicin/vincristine, ifosfamide/mesna, and doxorubicin/dacarbazine, but, to date, no controlled studies have been completed (Chamberlain, 2004). Recently, calcium channel blockers such as diltiazem and verapamil have also been used to augment hydroxyurea and RU486. Verotoxin, an *E. coli* toxin, has been shown to affect the Gb3 marker mostly on high-grade meningiomas. These substances are being used on a limited basis, and no long-term outcomes are available (Ragel, Gillespie, & Kushnir, 2006; Salhia, Rutka, & Lingwood, 2004).

Symptom Management

Patients with meningiomas, as with all brain tumors, may have symptoms related to the tumor or as side effects of treatment. Headaches, with or without nausea and vomiting, may be the result of cerebral edema and are treated with corticosteroids and analgesics. Seizures are medically managed with antiepileptic drugs. In addition, prophylactic use of antiepileptic drugs may be used perioperatively (Bohan, Gallia, & Brem, 2008).

Nursing Care

The role of the neurosurgical nurse in the care of patients with aggressive meningiomas is significantly different from that of patients with low-grade, benign meningiomas. Preoperative teaching focuses on attempts at complete surgical resection but also on the possible need for additional treatment, including RT. Postoperative and discharge planning reinforce the need for frequent monitoring with imaging studies and visits to the neurosurgeon, neurologist, or oncologist. If adjuvant RT is needed, a discussion of treatment objectives, timing, side effects, and follow-up monitoring is essential.

When RT or further surgery is indicated for residual or recurrent high-grade meningioma, nursing education will focus on potential wound-healing problems. Scrupulous wound care and frequent monitoring by the caregiver are essential to improving patient outcomes (Bohan et al., 2008). Although long-term survival is anticipated and even expected in many cases, it is important to reassure the patient that he or she will have careful monitoring and that further treatment may be needed and is of significant benefit.

Summary

Most intracranial meningiomas are benign, requiring monitoring or surgical resection with no further therapy. For the small percentage of patients who harbor more aggressive meningiomas, their course may involve surgery, RT, and, in some cases, medical therapy and clinical trials. Not only is the length and complexity of treatment impacted, but survival may be impacted as well. This is likely to be an unexpected outcome for the patient who expects the diagnosis of ''benign'' meningioma. The neuroscience nurse aids the patient during this process and is an integral member of the multidisciplinary team, providing clinical care, patient and family education, and ongoing support.

References

Akutsu, H., Sugita, K., Sonobe, M., & Matsumura, A. (2003). Parasagittal meningioma, en plaque with extracranial extension presenting diffuse massive hyperostosis of the skull. *Surgical Neurology*, *61*, 165–170.

Bohan, E. M., Gallia, G. L., & Brem, H. (2008). Brain tumors. In E. Barker (Ed.), *Neuroscience nursing; A spectrum of care* (pp. 215–248). St. Louis, MO: Mosby Elsevier.

Bruna, J., Brell, M., Ferrer, I., Gimenez-Bonafe, P., & Tortosa, A. (2007). Ki-67 proliferative index predicts clinical outcomes in patients with atypical or anaplastic meningioma. *Neuropathology*, *27*(2), 114–120.

Burger, P. C., & Scheithauer, B. W. (2007). Tumors of the central nervous system (p. 331). Washington, DC: American Registry of Pathology and Armed Forces Institute of Pathology.

Central Brain Tumor Registry of the United States. (2004–2005). *Primary brain tumors in the United States. 1997–2001 Statistical report*. Hinsdale, IL: Central Brain Tumors Registry of the United States.

Chamberlain, M. C. (2004). Intracerebral meningiomas. *Current Treatment Options in Neurology*, *6*, 297–305.

Custer, B. S., Koepsell, T. D., & Mueller, B. A. (2002). The

association between breast carcinoma and meningioma in women. *Cancer*, *94*, 1626–1635.

Gosztonyi, G., Slowik, F., & Pasztor, E. (2004). Intracranial meningiomas developing at long intervals following low-dose x-ray irradiation of the head. *Journal of Neuro-Oncology*, *70*, 59–65.

Haddad, G. F., Al-Mefty, O., & Abdulrauf, S. (2004). Part VI: Extrinsic tumors—meningiomas. In H. Brem, & R. Sawaya (Eds.), *Youmans neurological surgery* (5th ed., Vol. 1, pp. 1099–1131). Philadelphia: Saunders.

Hancq, S., Salmon, I., Brotchi, J., & Al, E. (2004). S100A5: A marker of recurrence in WHO grade I meningiomas. *Neuropathology and Applied Neurobiology*, *30*, 178–187.

Figueroa, B. E., Quint, D. J., McKeever, P. E., & Chandler, W. F. (1999). Case report: Extracranial metastatic meningioma. *British Journal of Radiology*, *72*, 513–516.

Newton, H. B. (2007). Hydroxyurea chemotherapy in the treatment of meningioma. *Neurosurgical Focus*, *23*(4), E11.

Pasquier, D., Bijmolt, S., Villa, S., Krengli, M., Weber, D., Baumert, B., et al. (2007). *Atypical and malignant meningioma: Outcome and prognostic factors in 119 irradiated patients: A multicentre, retrospective study of the Rare Cancer network* [Abstract]. Paper presented at the 49th Annual ASTRO Meeting, Los Angeles, CA.

Perry, A., Scheithauer, B. W., Stafford, S. L., Lohse, C. M., & Wollan, P. C. (1999). ''Malignancy'' in meningiomas: A clinicopathologic study of 116 patients. *Cancer*, *85*, 2046–2056.

Perry, A., Stafford, S. L., & Scheithauer, B. W. (1997). Meningioma grading: An analysis of histologic parameters. *American Journal of Surgical Pathology*, *21*(12), 1455–1465.

Phillips, L. E., Koepsell, T. D., VanBelle, G., Kukull, W. A., Gehrels, J. A., & Longstetch, W. T., Jr. (2002). History of head trauma and risk of intracranial meningioma: Population-based case-control study. *Neurology*, *58*, 1849–1852.

Phillips, L. E., Frankenfeld, C. L., Drangsholt, M., Koepsell, T. D., VanBelle, G., & Longstretch, W. T., Jr. (2005). Intracranial meningioma and ionizing radiation in medical and occupational settings. *Neurology*, *64*, 350–352.

Ragel, B. T., Gillespie, D. L., & Kushnir, V. (2006). Calcium channel antagonist augment hydroxyurea and RU-486-induced inhibition of meningioma growth in vivo and in vitro. *Neurosurgery*, *59*(5), 1109–1121.

Rosenberg, L. A., Prayson, A., Lee, J., Reddy, C. A., Chao, S. T., Barnett, G., et al. (2007). Long term experience with WHO III meningiomas at the Cleveland Clinic Foundation [Abstract]. *International Journal of Radiation Oncology, Biology, Physics*, *69*(3), S256.

Salhia, B., Rutka, J. T., & Lingwood, C. (2004). The treatment of malignant meningioma with Verotoxin. *Neoplasia*, *4*(4), 304–311.

Sandhyamani, J. E., Rao, S., Nair, S., & Radhakrishnan, V. V. (2000). Atypical meningioma: A clinicopathological analysis. *Neurology India*, *48*(4), 338–342.

Schulz-Ertner, D., Milker-Zabel, S., Thilmann, C., & Debus, J. (2005). Results of radiation therapy in atypical and anaplastic meningiomas. *International Journal of Radiation Oncology, Biology, Physics*, *63*(Suppl. 1), S263.

Shaw, R., Kissun, D., Boyle, M., & Triantafyllou, A. (2004). Primary meningiomas of the scalp as a late complication of skull fracture: Case report and literature review. *International Journal of Oral and Maxillofacial Surgery*, *33*(3), 509–511.

Takahashi, J. A., Ueba, T., & Hasimoto, N. (2004). The combination of mitotic and Ki-67 indices as a useful method for predicting short-term recurrence of meningiomas. *Surgical Neurology*, *61*(2), 49–155.

Wen, P. Y., & Drappatz, J. (2006). Novel therapies for meningiomas. *Expert Review of Neurotherapeutics*, *6*(10), 1447–1464.

Whittle, P. R., Smith, C., Navoo, P., & Collie, D. (2004). Meningiomas. *Lancet*, *363*, 1535–1543.

Willis, J., Smith, C., & Ironside, J. W. (2005). The accuracy of meningioma grading: A 10 year retrospective audit. *Neuropathology and Applied Neurobiology*, *31*(2), 141–149.

Zeltzer, P. M. (2004). *Brain tumors: Leaving the Garden of Eden* (pp. 291–305). Chicago: Shilysca Press.