Medical Management of Meningiomas

Current Status, Failed Treatments, and Promising Horizons

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KEYWORDS

• Targeted treatment • Meningiomas • Genetics • Medical management

KEY POINTS

- Meningiomas have the propensity for aggressive recurrence and resistance to traditional therapy.
- Only alpha-interferon, somatostatin receptor agonists, and vascular endothelial growth factor inhibitors are currently recommended for medical treatment of meningiomas.
- Novel therapeutic approaches and combinations may be a useful method in the treatment of aggressive meningiomas.

INTRODUCTION

Meningiomas are mostly benign tumors in adults that arise from the arachnoidal cap cells[1] intracranially and in the spine with an incidence of 7.44:100,000.[2] Most meningiomas are World Health Organization (WHO) grade I (80%); however, atypical grade II (15%–20%) and anaplastic grade III (1%–3%) tumors are relatively common and show a greater propensity for recurrence and therapeutic resistance.[3] Changes introduced in the 2007 WHO guidelines have led to an increase in the relative percentage of grade II and III meningiomas. Risk factors for meningioma include older age, a variety of genetic mutations and family disorders, ionizing radiation, head trauma, and sex.[1] Current therapeutic modalities include maximal safe gross total resection (GTR) followed by radiotherapy for higher-grade or recurrent lesions.[4] The Simpson grade, evaluating the degree of surgical resection, continues to be a viable tool for predicting survival and recurrence rates.[5] WHO grade II meningiomas show 5-year local control rates of 78% to 100% and 5-year progression-free survival (PFS) rates of 74% to 100% with GTR and radiotherapy.[6,7] WHO grade III meningiomas show 5-year PFS rates of 15% to 57% and 5-year overall survival (OS) of 47% to 61% with GTR and radiotherapy.[7] Although surgery and radiotherapy have been widely studied in the treatment and control of meningiomas, chemotherapeutic and targeted drugs have limited clinical efficacy.

The current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines, www.nccn.org) recommend radiological evaluation with biopsy if needed, as first-line steps in the evaluation of meningioma (**Fig. 1**). After radiographic or biopsy-proven diagnosis, asymptomatic meningiomas are recommended for surgery if they are accessible

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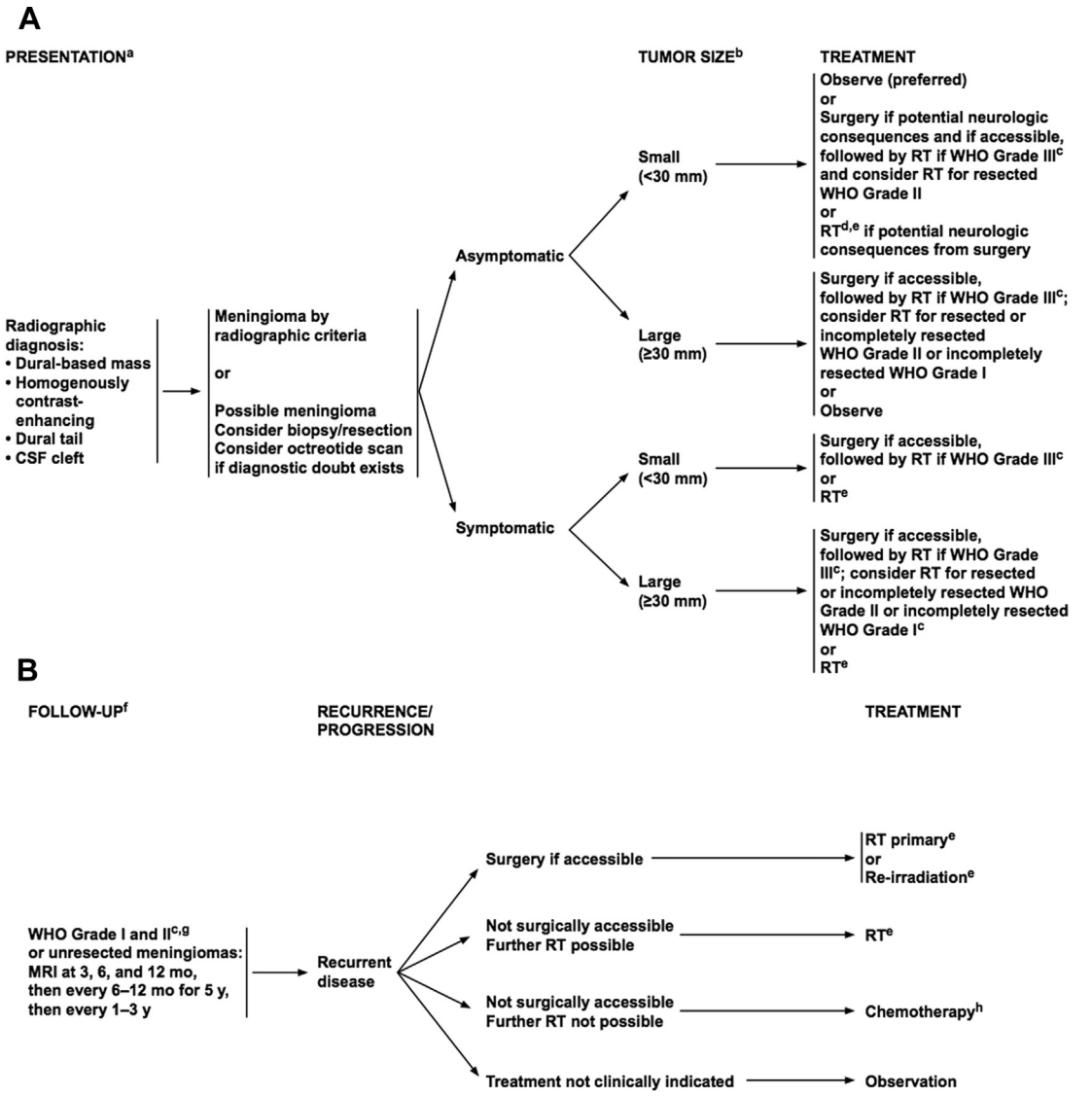

Fig. 1. NCCN guidelines version 1.2015: meningiomas. (*A*) Guidelines for the treatment of newly diagnosed meningioma. For small, asymptomatic lesions, observation is generally recommended after clinical and radiographic evaluation. For larger asymptomatic lesions, surgical resection is typically recommended, particularly when they are located in more accessible areas or there are potential neurologic consequences to a conservative approach. Depending on tumor grade, subsequent radiotherapy (RT) may also be recommended. Tumors that are symptomatic are referred for surgical resection when feasible. These patients are monitored closely after surgery and may undergo RT depending on tumor grade and level of resection. CSF, cerebrospinal fluid. (*B*) Guidelines for the treatment of recurrent meningioma. After treatment, patients are followed at 3, 6, and 12 months with contrast-enhanced MRI. After 1 year, the MRIs are repeated every 6 to 12 months for 5 years and then every 1 to 3 years. The management of recurrence depends on individual factors, personalized to the patient. For instance, surgical treatment followed by RT may be used if the recurrence is accessible, whereas RT or chemotherapy, or observation, may be recommended if the lesion is surgically inaccessible. [a] Multidisciplinary input for treatment planning if feasible. [b] The median growth rate for meningiomas is 4 mm per annum. [c] WHO Grade I = benign meningioma; WHO Grade II = atypical meningioma; WHO Grade III = malignant (anaplastic) meningioma. [d] RT can be either external-beam or stereotactic radiosurgery (SRS). [e] Principles of brain tumor radiation therapy: WHO grade I meningiomas may be treated by fractionated conformal radiotherapy with doses of 45 to 54 Gy. For WHO grade II meningiomas undergoing radiation, treatment should be directed to gross tumor (if present) and surgical bed + a margin (1–2 cm) to a dose of 54 to 60 Gy in 1.8 to 2.0 Gy fractions. Consider limiting margin expansion into the brain parenchyma if there is no evidence of brain invasion. WHO grade III meningiomas should be treated as malignant tumors with treatment directed to gross tumor (if present) and surgical