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Overview

Controversies in Radiotherapy for Meningioma

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Abstract

Meningiomas are the most common primary intracranial tumour. Although external beam radiotherapy and radiosurgery are well-established treatments, affording local control rates of 85–95% at 10 years, the evidence base is mainly limited to single institution case series. This has resulted in inconsistent practices. It is generally agreed that radiotherapy is an established primary therapy in patients requiring treatment for surgically inaccessible disease and postoperatively for grade 3 tumours. Controversy exists surrounding whether radiotherapy should be upfront or reserved for progression for incompletely excised and grade 2 tumours. External beam radiotherapy and radiosurgery have not been directly compared, but seem to offer comparable rates of control for benign disease. Target volume definition remains contentious, including the inclusion of hyperostotic bone, dural tail and surrounding brain, but pathological studies are shedding some light. Most agree that doses around 50–54 Gy are appropriate for benign meningiomas and ongoing European Organization for Research and Treatment of Cancer and Radiation Therapy Oncology Group studies are evaluating dose escalation for higher risk disease. Here we address the 'who, when and how' of radiotherapy for meningioma.
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Key words: Meningioma; radiosurgery; radiotherapy; review

Statement of Search Strategies Used and Sources of Information

A comprehensive review of published studies and review articles pertaining to radiotherapy for meningioma was carried out using PubMed. As the evidence base is level IV or V, all publications, regardless of study design, were considered. Ongoing Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer study protocols and the National Comprehensive Cancer Network guidelines related to meningioma were accessed via their respective websites.

Introduction

Meningiomas are the most common primary intracranial tumour [1]. Between 70 and 80% are benign and active surveillance with serial magnetic resonance imaging (MRI) can be appropriate for those without significant symptoms. In the largest analysis of growth in observed meningiomas (244 patients, mean follow-up 3.8 years), 74% showed growth on volumetric criteria (>8.2%) and 44% using linear criteria (≥2 mm), with 26.3% requiring treatment in this period [2].

Nevertheless, depending on location and grade, meningiomas can be severely disabling and can limit life expectancy. Surgery is the mainstay of therapy, as this offers the potential of cure, but tumour location may preclude meaningful resection. Figure 1 depicts the difference in surgical accessibility between meningioma sites. The Simpson grading scale describes the extent of surgical meningioma resection (Table 1) and is an important predictor of recurrence/progression [3]. Most authors (including the Radiation Therapy Oncology Group [RTOG] and the European Organization for Research and Treatment of Cancer [EORTC]) classify a gross total resection (GTR) as Simpson grade 1–3 (abnormal bone may remain). Tumour location prevents GTR in about a third of cases (about 50% in the skull base) [4,5].

External beam radiotherapy (EBRT) and radiosurgery are well-established treatments for meningioma. However, the

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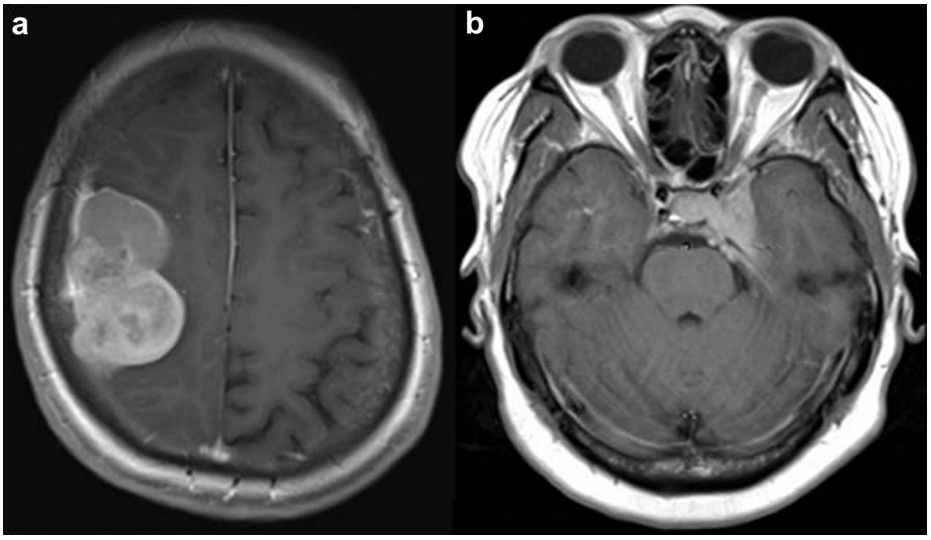

Fig 1. Tumour location and surgical potential. (a) Large convexity meningioma (gross total resection was possible); (b) smaller cavernous sinus meningioma (no meaningful resection possible due to proximity to vessels and nerves).

evidence base is limited to retrospective case series (usually single institution) that often analyse outcomes together regardless of treatment setting, technique or dose. Furthermore, many series have insufficient follow-up as progression/recurrence can occur even after 10 years. Local control rates 5–10 years after modern EBRT in benign tumours are generally >90% and recent radiosurgery series suggest similar results for local control [6]. Table 2 details outcomes for EBRT from series using exclusively modern radiotherapy techniques (not two-dimensional). Where possible, results are grouped for benign/non-benign tumours and according to treatment timing, but should be interpreted with caution in view of the small number of progressions and non-benign tumours in most series. Symptom control after radiation is not uniformly reported and analysis is clouded by high rates of previous surgery. However, some degree of clinical improvement is reported in 29.3–53.5% of patients after EBRT/radiosurgery, with symptom stabilisation in most others with radiological stable disease [16,22–26].

Table 1
Simpson grading: extent of meningioma resection

Simpson grade	Description
1	Macroscopically complete tumour removal with excision of the dural attachment and any abnormal bone
2	Macroscopically complete tumour removal with coagulation of its dural attachment
3	Macroscopically complete removal of the intradural tumour without resection or coagulation of its dural attachment or extradural extensions
4	Subtotal removal of the tumour
5	Simple decompression of the tumour

Pathology

Meningiomas are broadly categorised as grade 1 (benign) and grade 2 and 3 (non-benign), but there are a multitude of pathological subtypes and molecular features within each grade and considerable interobserver variability in grading. This complicates outcome analyses. Biopsy is usually unnecessary when tumours are adjacent to critical structures, as MRI is usually diagnostic. However, tumour grade cannot be reliably identified on imaging [27], which may have implications for radiotherapy and the interpretation of outcomes. That said, biopsy is unlikely to identify small high-grade regions or brain invasion, a feature that confers grade 2 status on meningiomas since the World Health Organization (WHO) 2007 classification revision. This revision may result in a stage migration in treatment outcomes in new studies (most series include patients diagnosed pre-2007).

Therefore, although radiotherapy seems to be an effective treatment for meningioma, the poor evidence base means that many controversies exist, which we discuss in this review.

When Should Radiotherapy be Used?

Primary Radiotherapy

EBRT or radiosurgery is used in the primary setting in symptomatic patients when significant resection is not possible, usually because the meningioma involves critical structures [28]. Durable progression-free survival (PFS) is experienced by most patients, although older studies with longer follow-up periods usually show lower PFS rates [29]. It is unclear whether PFS after radiotherapy is influenced by previous surgery. Some studies report no difference between groups: Tanzler *et al.* [20] recently reported 5 and 10 year PFS of 99 and 97%, respectively, for patients with grade

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