Stereotactic Radiosurgery for Skull Base Meningiomas

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Abstract

Complete resection of meningiomas occurring at the skull base may be difficult, due to the proximity of critical neurovascular structures. Due to the benign nature of these lesions, most patients with skull base meningiomas have an extended life expectancy. The goal of treatment for these lesions, therefore, revolves around long-term tumor control without worsening neurological function. Stereotactic radiosurgery is one of three main treatment options for the treatment of cranial base meningiomas, and has been shown to have similar rates of tumor control with safe administration within 3–5 mm of cranial nerves and brainstem. In this chapter, we review the literature reporting outcomes following use of stereotactic radiosurgery for these lesions, and the rationale for decision-making about treatment for these lesions.

Introduction

Meningiomas occurring at the skull base represent a neurosurgical challenge. Although most often histologically benign, these tumors typically continue to grow unless treated, and cause symptoms due to compression of cranial nerves, vessels or through mass effect. The location of these tumors at the skull base, with the close proximity of vital neural and vascular tissues, makes complete surgical resection according to

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the principles of oncological cure difficult. Presence of tumor in the cavernous sinus, associated with the ICA and/or optic nerves and chiasm, or extending along the dura of the anterior or middle cranial fossae, all represent instances in which complete surgical resection may be associated with an unacceptably high risk of morbidity. Because of this, treatment aimed at achieving local control of tumor growth with relief or stabilization of neurological deficits has been increasingly investigated.

External beam radiation therapy and stereotactic radiosurgery (SRS) are two logical treatment options within this altered paradigm of treatment for skull base meningiomas. Meningiomas have been an obvious target for SRS due to their clear demarcation from surrounding neural tissue and bone on modern imaging modalities. The rationale for treatment is to provide long-term control with a lower risk of damage to surrounding structures due to a rigorous planning algorithm with sharp drop-off of radiation dose at the margin of the tumor. Radiosurgery, as originally conceived in the 1950s by Leksell, combined the principles of radiotherapy with stereotactic neurosurgery to provide a precise focus of radiation via gamma rays in a predetermined trajectory in 3-dimensional space. The intersection of small-diameter beams allows focused delivery of radiation with a sharp fall-off of dose gradient outside the target (Vesper et al., 2009). Today, a number of different radiosurgical systems are available that incorporate both framed and frameless stereotactic delivery. A detailed review of these is beyond the scope of this chapter, but results from each system appear to be similar, and differentiation between systems will require rigorous comparative studies with long-term follow up (Andrews et al., 2006). The stereotactically modified linear accelerator (LINAC), protons, and gamma knife modalities have been historically most widely used. CyberKnife is a frameless radiosurgical system that uses inverse planning with non-isocentric radiation delivery, and represents another option for delivery of stereotactic radiosurgery in one or more fractions (Adler et al., 1997). Though all systems achieve precise stereotaxy, framed systems may provide peace of mind in the localization of high doses of radiation near the cranial nerves at the skull base.

General Principles

Stereotactic radiosurgical principles began to be applied to skull base meningiomas in the early 1990s (Starke et al., 2012). As radiosurgical treatment has evolved, with improved conformality and more predictable dose fall-off, smaller doses have been used in order to minimize long-term toxicity while maintaining efficacy. It is possible to maintain therapeutic doses to the tumor with highly accurate conformality, using multiple isocenters of different size and configuration, with differential weighting and selective beam blocking. Practical guides to creating radiosurgical plans for irregularly shaped skull base tumors have been recently published (Kondziolka et al., 2008a). The radiation tolerance of the cranial nerves and optic apparatus continue to be a subject of debate, particularly in the setting of multisession radiosurgical plans using CyberKnife, Novalis, and Gamma Knife Extend systems (Leber et al., 1998; Tuniz et al., 2009). Although individual treatment planning varies with the precise characteristics of each tumor, some general guidelines are outlined below, bearing in mind that in modern series, doses of 12–14 Gy have been shown to be as effective as larger doses, while allowing limited exposure of sensitive structures:

1. The optic nerve and apparatus should not receive more than 10–12 Gy; some groups aim for <8.5 Gy to the optic apparatus, and the target may be more safely 8–10 Gy depending on the volume of nerve involved.
2. For the brainstem, there is little reliable data but doses ≤15 Gy appear to be reasonable.
3. Tumor margin dose at the CPA should be 12–13 Gy at most, with lower limits for patients in whom hearing preservation is the goal of treatment.
4. Limits of 12–14 Gy have been used around other cranial nerves without high incidence of post-radiosurgical deficits.

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Anterior and Middle Cranial Fossa Meningiomas

SRS may be used either as a primary treatment option or as an adjuvant therapy following surgical resection. After using GKS as a primary treatment option, rates of local control vary from 85 to 98 % at 5 years, and 73 to 97 % at 10 years (Starke et al., 2012). In a combined series of meningiomas at different intracranial locations, tumor control of 93 % at 5 years and 87 % at 10 and 15 years was reported (Kondziolka et al., 2008b). Actuarial 5- and 10-year control rates of 91 and 87.6 %, respectively, were reported in a recent systematic review of GKRS for skull base meningiomas (Minniti et al., 2009). The reported rates of tumor shrinkage vary widely, between 8 and 66 % depending on series. In the majority of cases, tumor volumes remain stable, with a minority of patients experiencing either tumor shrinkage or expansion on long-term follow up imaging.

In a large cohort study, there were no differences in long-term survival between 384 patients treated with postoperative SRS compared with 488 patients who underwent primary SRS (Kondziolka et al., 2008b). Factors associated with poorer outcome include larger tumor volumes, inadequate conformity index, and tumor recurrence. For larger tumors, there may be a tendency to formulate more conservative treatment plans due to closer association with radiosensitive structures, thus resulting in lower control rates. In either case, location is obviously of paramount importance in predicting the tumor response and risk of cranial neuropathies. Tumors located in the cavernous sinus may be more likely to improve after radiosurgery than at other skull base locations.

The risk of neurological complications ranges between 3 and 40 % depending on series, most commonly in the range of 3 % for transient and 5 % for permanent neurological complications. There is a risk of secondary neoplasia developing after radiosurgery, but this is rarely observed in retrospective or prospective series. The reported incidence is 0–3 per 200,000 patients (Starke et al., 2012), which is similar to the rate of spontaneous development of cancer in the general population. Though the absolute risk is low, it should be considered particularly for young patients with slow-growing, benign processes such as skull base meningiomas. If cranial neuropathies develop, after radiosurgical treatment, from tumor progression, it is an indication that inadequate radiation has been dosed to the tumor margin. The optic apparatus, for example, has generally been limited to a dose of 8–10 Gy, but if markedly lower doses are administered in an attempt to limit morbidity, there is a risk of inadequate tumor control.

SRS may be used in the setting of regrowth after previous treatment. Conservative treatment remains a primary option, especially for older patients who experience growth of a previously treated meningioma, whether treated by primary surgical or radiosurgical means. Radiosurgery does not make subsequent resection more technically challenging. Alternatively, SRS may be attempted again, although growth at this location often makes planning more difficult due to the close proximity of cranial nerves and vessels and the likelihood that these structures have already been exposed to radiation during previous treatments.

Posterior Fossa Meningiomas

Many of the issues surrounding use of SRS at the anterior skull base also apply to the treatment of posterior fossa meningiomas. Proximity of these lesions to the brainstem, as well as venous sinuses and prominent vessels, makes surgical resection difficult, although some degree of microsurgical resection may be essential to relieve mass effect or hydrocephalus. Rates of complete surgical resection vary from 40 to 96 %, with morbidity and mortality ranging from 0 to 13 % and 13 to 40 %, respectively (Starke et al., 2011). As with other skull base meningiomas, there has been an increasing recognition that preservation of neurological function may be best achieved through a

more conservative surgical approach, combined with adjuvant radiation therapy or radiosurgery. Particular to the posterior fossa, it is essential to limit the radiation exposure of the brainstem to ≤12 Gy, as these doses even at volumes as low as 0.1 cm^3 have been shown to result in new neurological deficits (Sharma et al., 2008). Likewise, SRS has been used successfully as a primary treatment in certain circumstances. Because of the lower incidence of posterior fossa meningiomas compared to those occurring at other skull base locations, reports of these lesions in the literature often combine a variety of skull base locations (including sellar, sphenoid, cavernous sinus, olfactory groove, optic sheath and foramen magnum). In our experience treating posterior fossa meningiomas with primary SRS, 36 % had no change in tumor volume, and 51 % had a decrease at last follow-up, with 91 % of patients experiencing stable or improved clinical symptoms (Starke et al., 2011). Characterization of long-term tumor control following primary SRS, as well as the potential neurocognitive effects of radiosurgery at and around the brainstem, require ongoing investigation. SRS remains, however, a viable alternative for primary treatment in patients who are poor surgical candidates, and as an alternative to radiotherapy for residual or recurrence after primary surgical resection.

Comparison with Surgical Resection and Radiotherapy

Historically, the gold standard for meningiomas at any intracranial location has been total resection along with the dural tail and any involved bone. This can be impossible to achieve in practice, contributing to the observation that these lesions tend to recur after surgery. Resection or biopsy are the only options that offer the potential for formal histological diagnosis of skull base meningiomas. Though these lesions have a characteristic appearance on MR/CT imaging, there are other pathologies that may occur in this area and that may mimic the appearance of meningioma, which would be the target of different treatment strategies. Additionally, the finding of a more aggressive histological grade than WHO Grade I meningioma warrants consideration for adjuvant radiotherapy even in the setting of gross total resection.

A variety of skull base approaches have been developed, and long-term control after Simpson Grade I resection is very high (Linskey et al., 2005; Pollock et al., 2003), but achieving this can be extremely difficult without risking significant morbidity. Gross total resection rates range from 20 to 87.5 % (Bassiouni et al., 2006; Chi and McDermott, 2003; Otani et al., 2006; Sanna et al., 2007; Voss et al., 2000). In earlier surgical series, postoperative complication rates were high (on the order of 30–40 %), with mortality of up to 7 %. More recent series report much lower complication rates. Along with improvements in microsurgical technique, incorporation of stereotactic planning and intraoperative monitoring and imaging, there may be an increasing comfort with the concept of leaving residual tumor to be treated with adjuvant therapies such as SRS. Combining microsurgery with SRS appears to improve long-term local control rates, with 5-year control rates of upwards of 90 % (Davidson et al., 2007; Duma et al., 1993; Ichinose et al., 2010; Iwai et al., 2001, 2008; Lunsford, 1994; Zachenhofer et al., 2006). Again, the precise location of the lesion is important in treatment planning. For instance, for a parasellar meningioma involving both intra- and extra-cavernous locations, a microsurgical approach for the extracavernous lesion and radiosurgical approach for the intracavernous portion may offer the greatest potential for reduction of tumor burden with minimal risk of neurovascular injury (Williams et al., 2011).

Radiotherapy represents a third treatment option for skull base meningiomas. As with fractionated SRS (see below), dividing radiotherapeutic treatment may allow time for normal tissue to heal between treatments. In fact, modern stereotactic radiotherapy is very similar to SRS, utilizing similarly precise dose localization and steep dose gradients. The major difference is the number of fractions, and the total delivered radiation dose. A variety of regimens have been employed, most commonly delivering 50–55 Gy over 30–33 fractions. Five and ten-year local control rates

range from 75 to 95 % in different studies; actuarial combined control rates are 90 % at 5 years and 83 % at 10 years (Condra et al., 1997; Dufour et al., 2001; Elia et al., 2007; Goldsmith et al., 1994; Hasegawa et al., 2007; Mendenhall et al., 2003; Nutting et al., 1999). Symptomatic improvement is reported in 69–100 % (Dufour et al., 2001; Maire et al., 1995; Mendenhall et al., 2003; Nutting et al., 1999), but complications occur in up to 24 % of cases (Minniti et al., 2009). Cranial nerve injury, including radiation injury to the optic apparatus, occurs in 0–3 % of cases. Newer techniques such as intensity-modulated radiotherapy and stereotactic radiotherapy use smaller treatment volumes and image guidance, and have demonstrated safety in and around the skull base. Overall, outcomes and toxicity are both very similar between fractionated SRT and SRS (Elia et al., 2007). The rate of permanent treatment-related morbidity is similar to that seen after SRS, and is reported at 0–3 % (Lo et al., 2002; Metellus et al., 2005). In addition to neurological deficits as discussed above, toxicity includes fatigue, skin erythema and alopecia.

Decision Making in Treatment of Skull Base Meningiomas

The selection of appropriate treatment for patients with presumed or histologically proven skull base meningiomas should be undertaken with the goal of achieving long-term tumor control without additional neurological morbidity. Patients should initially be evaluated in a center with expertise in neurosurgery, radiosurgery and radiation oncology. Decisions should always be made in a multidisciplinary fashion and must be individualized based on imaging characteristics, anatomic features, tumor location, size, and patient preference. For patients with large skull base tumors who present with neurological deficit or symptoms from mass effect, microsurgical resection is the initial treatment of choice, as it allows histological diagnosis and relief of compression with the potential for some neurological recovery. SRS may be appropriate as a primary or adjunctive treatment for a variety of skull base meningiomas, as outlined above. One approach, which we have found to be effective and well tolerated, has been to limit the use of SRS to tumors <3 cm in diameter, with 3–5 mm margin between the tumor limit and radiosensitive skull base structures. Fractionated SRT may be best suited for instances in which SRS is limited, such as for larger lesions, or for optic nerve sheath lesions (Elia et al., 2007). Finally, a more conservative approach of careful observation may be the best option for some older patients with small skull base meningiomas.

The development of frameless radiosurgical alternatives has led to the investigation of staged or "hypofractionated" radiosurgery, which may also be useful for skull base meningiomas. Theoretically, fractionation allows differentiation of response between abnormal tumor tissue and surrounding normal neurovascular structures. Assuming that normal tissue recovers faster from the toxic effects of radiation, fractionation may allow the delivery of slightly lower radiation doses over time while maintaining a cumulative "radiosurgical" effect. Benign tumors at the skull base, including a number of meningiomas, have been treated using this treatment strategy with high rates of tumor control and low morbidity, albeit in small series to date (Adler et al., 2006). Characterization of the optimal lesions for treatment with staged radiosurgery remains to be fully elucidated.

Conclusions

Stereotactic radiosurgery is a safe and effective treatment option, either as primary or adjuvant therapy, for skull base meningiomas. Neurological preservation and control of symptoms may be more commonly observed after radiosurgical treatment of petroclival, parasellar, and cerebellopontine angle lesions than at other anterior skull base locations. Lesions larger than 3 cm in diameter, or <3 mm from the optic apparatus, may be more safely treated with fractionated treatments, be they radiosurgical or radiotherapeutic. Overall rates of tumor control are comparable between SRS, SRT and microsurgery.

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