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Meningiomas of the cranial base

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Summary

Treatment objectives for meningiomas of the cranial base include relief of neurologic disability and prevention of clinical progression or recurrence with the least morbidity. Recent advances in skull base surgical techniques, through an appreciation of skull base anatomy and institutional specialization, have contributed major improvements to the outlook for patients with these tumors, and previously inoperable cases may now often be removed completely with acceptable risk. Since significant morbidity may be incurred during surgical resection of these difficult lesions, especially in terms of cranial nerve dysfunction, the value of aggressive surgical resection must be weighed against the often indolent natural history of these lesions, and must be individualized in each patient. Completeness of resection is the major prognostic factor determining the outcome of patients with typical benign meningiomas in terms of length of survival, risk of recurrence, and neurological disability. Various means of prognosticating the growth potential of a given tumor are being investigated, though none have yet been confirmed for their predictive value in typical, histologically benign meningiomas. The role of external beam radiotherapy has not been subjected to adequately controlled, prospective studies, and there is currently insufficient followup to assess the risks and benefits of stereotactic radiosurgery.
Advances in the clinical management of tumors of the skull base has had perhaps the greatest impact for patients with meningiomas who constitute a large portion of tumors seen in these locations. Although the majority have benign histological features, skull base meningiomas can present a formidable challenge due to their proximity to vital structures, surgical inaccessibility, and occasional aggressive features. The combination in recent years of advances in skull base surgical techniques, adjuvant therapy, and rehabilitation methods have dramatically improved the outcome for these tumors.

Historical perspective

The tumors of the meninges were described by a diverse nomenclature prior to the use of the term meningioma by Cushing in 1922 [1]. Historically, the first reported successful removal of a meningioma was that of a basal tumor of the sinciput by Zanobi Pecchiolo in 1835, with the patient being followed for two years [2]. Durante subsequently removed an olfactory groove tumor 'the size of an apple' in an operation lasting one hour [3]. The patient survived over 20 years, requiring one reoperation for recurrence at 11 years, and was presented in the United States at the International Medical Congress in 1887. Perhaps the most important early contribution to the field came with the publication of Cushing and Eisenhardt's widely cited monograph on meningiomas in 1938 [3, 4], containing many ob-

servations that still remain of interest and controversy today.

Meningiomas constitute about 15 to 20% of all primary brain tumors when large neurosurgical series are combined [5–7], with 33% to 50% of them occurring in skull base locations [9–13]. Nakasu [8] found meningiomas as an incidental finding in 2.3% of 10,033 autopsies, a reflection of their often benign evolution. The relevant sites of induction are related to the presence of arachnoidal cap cells in granulations where CSF resorption occurs, particularly along the major venous sinuses and their tributary veins, as well as around bony foramina for exiting vascular and nervous structures. Arachnoidal cap cells are felt to be a neural crest derivative, a feature relevant to the finding of other types of associated tumors in the syndrome of central or Type II neurofibromatosis (NF2) [14–17]. A candidate gene for this disease has been isolated recently, and may be relevant as tumor suppressor specific to meningiomas and related neoplasms [18].

Biological and pathological features

Pathology

The most widely used pathological description of these tumors is a modification of the terminology used by Cushing and Eisenhardt. The fibrous, syncytial (or meningotheliomatous), transitional, and angioblastic varieties make up the vast majority of cases. Other subvariants include tumors demonstrating psammomatous, microcystic, myxoid, xanthomatous, lipomatous, granulomatous, or secretory differentiation [5, 6]. The papillary variety has been associated with a higher incidence of malignant behavior and metastases [19, 20]. The hemangiopericytoma of the meninges (sometimes included under the term angioblastic meningioma) has also been found to have a more malignant natural history, and hemangiopericytic and papillary features may be found together in the same tumor [19, 21–23]. These more aggressive tumors are responsive to radiotherapy, which can lengthen disease free survival [24, 25].

Growth characteristics

Even when histologically indistinguishable, individual skull base meningiomas can have highly variable natural histories ranging from rapidly growing and invasive to slow-growing and indolent. The ability to predict a given tumor's clinical behavior would be of obvious value for the clinician making patient management decisions. For histologically benign meningiomas, the only clear risk factor for recurrence is extent of resection, though researchers have looked for markers of aggressive growth potential. Atypical, papillary, or angioblastic tumors have histological features which distinguish their more aggressive behavior [5, 6]. de la Monte [26] has identified several features of meningiomas with benign histology that were correlated to recurrence or decreased progression-free survival.

Additional predictive information may come from studies of markers for proliferative potential such as flow cytometry and bromodeoxyuridine labelling index. Flow cytometry of archival tissue was analyzed by May [27] in 40 patients undergoing complete resection of their tumors. Twenty patients were recurrence-free at an average follow up of 11.4 years, and 20 had recurrence documented radiographically at a mean interval to recurrence of 7.5 years. Tumors which recurred had a statistically significant difference in proliferative index compared to those which did not. The proliferative index was never above 19.2% in nonrecurrent tumors, but was greater than this value in 2/3 of the recurrent tumors. There appears to be little sampling error with this technique [28].

Bromodeoxyuridine labelling has also been used to examine biological behavior, with labelling indices correlated to radiographic doubling time, cell kinetics in culture, and histological features of atypia [29–31]. This vital procedure precludes examination of archival tissue and therefore the initial labelling index is not known for many recurrent tumors that were not previously examined at their first presentation. Correlation with histology has not been conclusively demonstrated as Lee [32] found that the labelling index was unremarkable (less than 1%) in 87% of histologically malignant meningiomas. Shibuya [33] examined 53 meningio-

mas, selected because their bromodeoxyuridine labelling index was ≥ 1%, and found a positive correlation between labelling index and both malignant histology and likelihood of recurrence. Of the tumors which did not recur during the study, none had a labelling index > 5%. Of the eight tumors with a labelling index ≥ 5%, all were recurrent at the initial analysis or recurred during the study period. Two of the 31 primary tumors recurred during the study period, however the labelling index was not helpful in predicting recurrence as neither tumor had an excessively high index. This technique has yet to be validated in a prospective fashion, but the ease and availability of bromodeoxyuridine labelling techniques will hopefully hasten its clinical validation. The ability to predict tumor growth rates through the use of these types of indices will be valuable for the often difficult decision making process in patients who may be elderly, minimally symptomatic, or have technically difficult lesions.

Biologic features

A variety of biological and clinical features of meningiomas, including etiologic factors, molecular genetics, and sex hormone and growth factor responsiveness, amongst others, have been discussed extensively in recent reviews [34–36].

Risk factors

Several risk factors or possible etiologic agents have been associated with meningioma induction. A history of significant head trauma was noted in nearly one-third of Cushing's patients [3, 4], and numerous reports of foreign bodies and other stigmata of trauma at sites of meningioma formation exist [37–39]. Annegers [40] reviewed the incidence of brain tumors in 2953 patients with significant head trauma and found that the four tumors occurring in the group did not exceed the expected incidence, though others have questioned this conclusion. Overall, the frequency of these types of reports leaves the issue intriguing but unresolved.

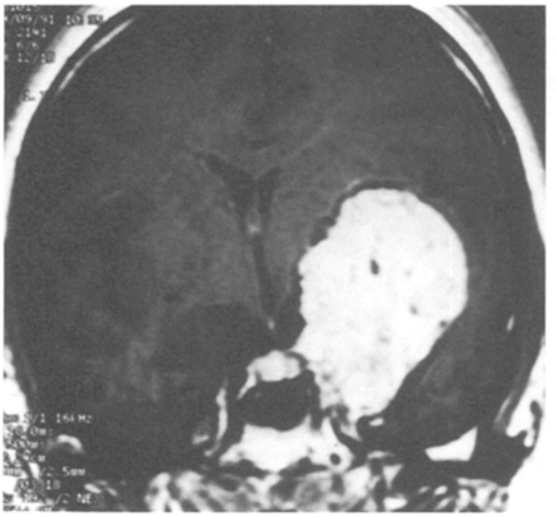
A prior history of radiation has been well demonstrated as a risk factor for meningioma formation. A higher incidence of meningioma has been found in large studies of patients receiving low dose irradiation for tinea capitis [49, 50], as well as smaller series of patients receiving high dose irradiation [51, 52]. Modan [49] studied a population of roughly 11000 children for 12 to 23 years following low dose radiation for ringworm and found a four-fold higher incidence of meningioma. These tumors occurred less often at the skull base, presumably because of the field used. Meningiomas of the skull base, however, have been associated with a prior history of full mouth dental X-ray studies [38, 39]. Overall, radiation induced tumors tend to have more atypical or anaplastic features histologically [53, 54], and are more often multiple [51, 52] or recurrent. Such characteristics may be important considerations in the management of radiation-induced meningiomas of the skull base. Iacono [52] found the latency of induction in patients receiving high doses (2000 to 7000 cGy) averaged 20.8 years, with a range of 12 to 27 years. Rusyniak [55] has reported a tumor induced three and one-half years after therapeutic radiation, and one patient in Mack's series developed a tumor five years following radiotherapy [51].

Molecular biology

Monosomy of chromosome 22 in meningiomas is one of the most characteristic genetic alterations observed among human solid tumors, and genotypic analysis reveals such abnormalities in up to 80% of cases [41]. This has suggested a mechanism of tumor induction involving loss of tumor suppressor genes located on chromosome 22. Additionally, a common mechanism for the formation of acoustic neuromas, spinal ependymomas, and meningiomas is suggested by their occurrence in the syndrome of central neurofibromatosis [14, 15]. All of these tumors share a common aberration in a region on chromosome 22 that has been implicated in the formation of sporadic meningiomas [17]. Recent cloning of a candidate gene for this disease [18], known as 'merlin', may reveal a common tumor suppressor mechanism in the formation of these related neoplasms.

Hormonal influence

A large literature regarding the involvement of sex



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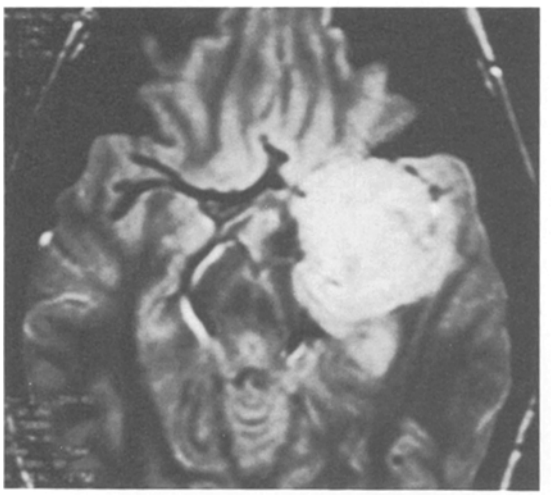

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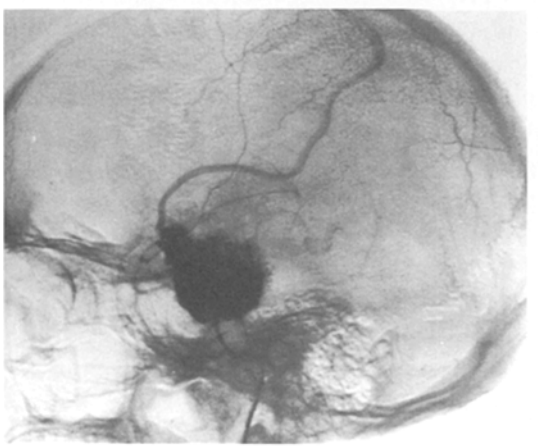

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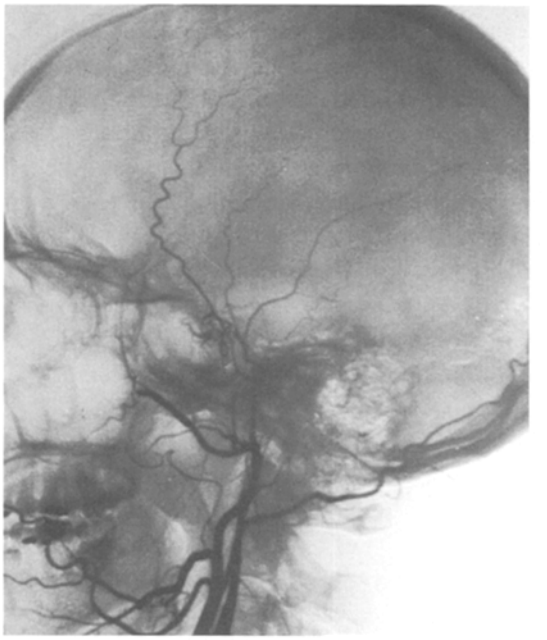

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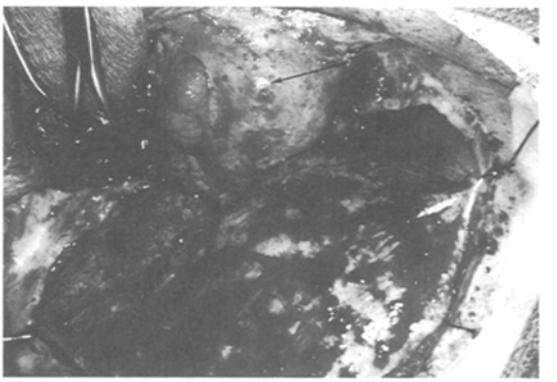

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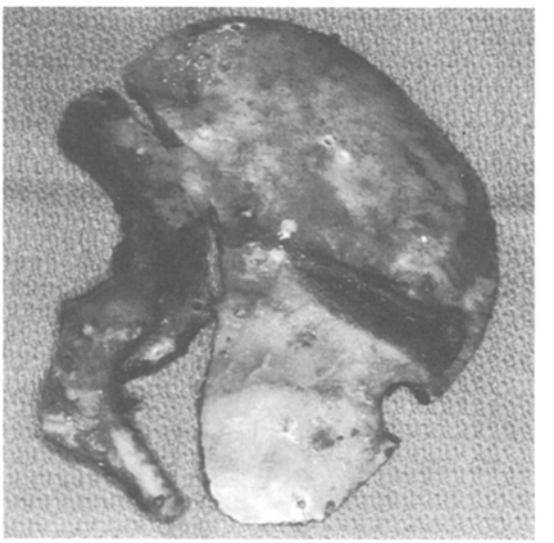

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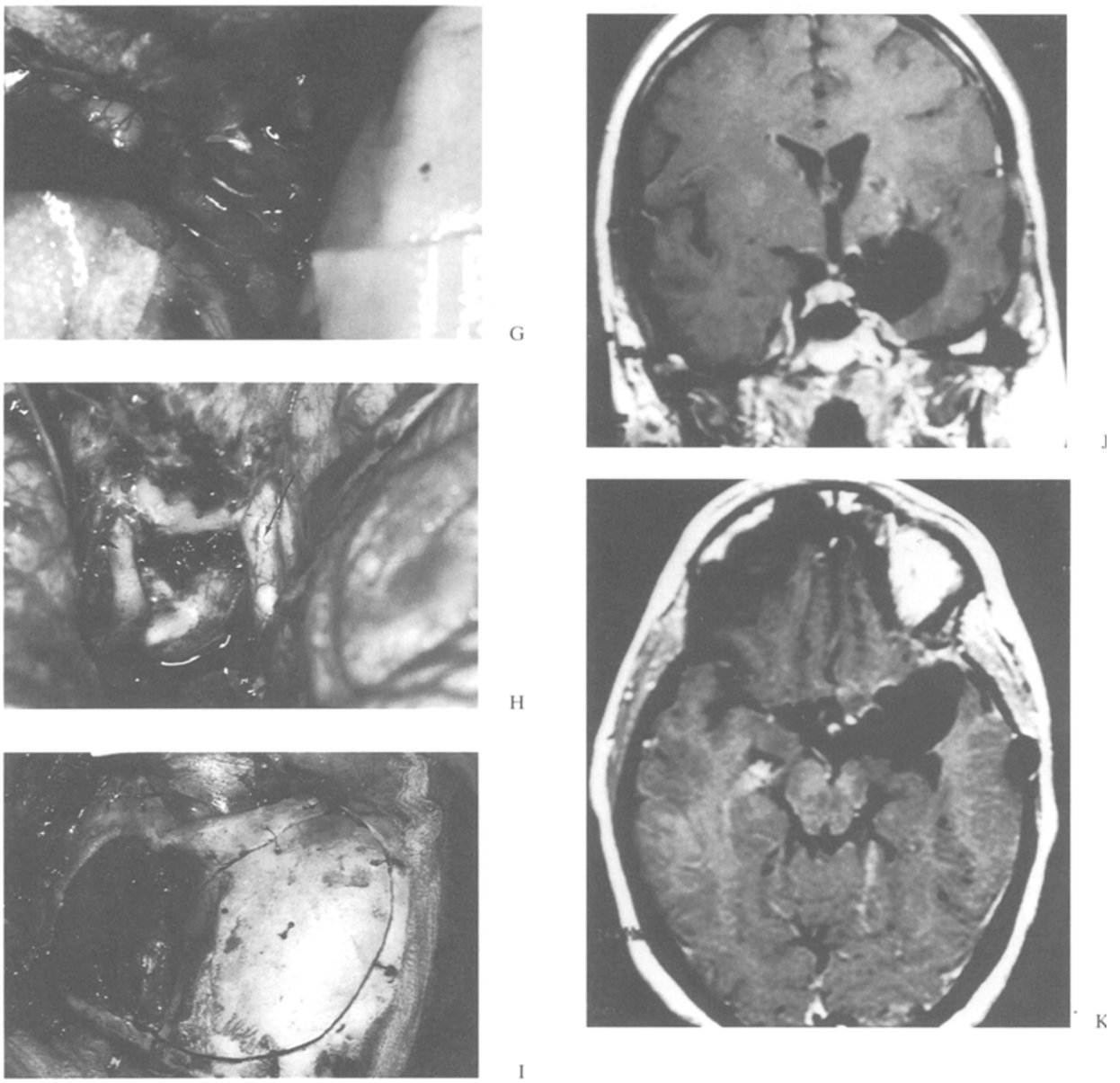


Fig. 1. (A) Coronal and (B) axial MRI of a large medial sphenoid wing meningioma involving the cavernous sinus. (C) Lateral angiogram shows marked vascular tumor blush supplied by a meningeal artery. (D) Angiogram demonstrating decreased vascularity following embolization. (E) Operative photograph following frontotemporal craniotomy and orbitozygomatic osteotomy. The periorbital fat is visible following unroofing of the orbit (arrow). (F) Operative photograph showing the frontotemporal bone flap and the orbitozygomatic osteotomy bone piece. (G) Operative photograph shows meningioma after Sylvian fissure has been split, with large blood vessel on its surface. (H) Operative photograph following gross total resection of tumor and cavernous sinus dissection. The optic nerve (arrow) and oculomotor nerve (arrowhead) are visible. (I) At the completion of the operation the bone pieces are wired back into place. (J) Coronal and (K) axial MRI one year postoperatively shows no evidence of tumor.

hormones in the pathogenesis of meningiomas exists, and has been well summarized in recent reviews [34]. The functional role of estrogen receptors in these tumors has been questioned, and the disappointing initial trials of tamoxifen therapy appear to bear this out [42, 43]. Studies of progesterone receptor status and responsivity of these tumors appears to indicate a more important role for

progestins in tumor growth [34, 42]. Trials with the anti-progestational agent RU-486 have been initiated based on these studies, and Grunberg [44] has found some improvement in five of a series of twelve patients treated for at least six months with the drug. Other reports exist suggesting the significance of androgens, glucocorticoids, dopamine-agonists, and various growth factors such as platelet-derived growth factor [45–48]. To date, none have been conclusively implicated in growth of meningiomas *in vivo*.

Radiographic features

The preoperative radiographic evaluation of meningiomas was historically based on plain skull films and angiographic appearance. Hyperostosis, intracranial calcification, or bone 'blistering' were useful diagnostic features. Cerebral angiography has contributed significantly to the understanding of the vascular supply of tumors in various locations, although its diagnostic role has been largely supplanted by MRI and CT. Angiography is primarily of benefit as an adjunct to surgery through preoperative embolization, or in assessing flow dependency via balloon occlusion testing in cases of basal tumors involving the carotid artery [56].

The development of CT and MRI scanning with intravenous contrast have been important advances in the diagnosis of skull base meningiomas and detailing the anatomical relationships with adjacent vital structures. The typical appearance of these lesions is that of an isodense to slightly hyperdense dural based lesion on CT, or an iso- to slightly hypointense appearance on T1-weighted MRI, with uniform contrast enhancement [57]. Peritumoral edema can be variable and is best seen on T2-weighted imaging. MRI is useful for assessing the patency of the dural sinuses [58] as well as the location or encasement of major vessels. MRI has considerable advantages over CT for imaging tumors of the posterior fossa and skull base due to the absence of bone artifact. Some degree of correlation can be made with histological or aggressive characteristics using MRI [58–60] or CT [61]. Differential diagnostic considerations are probably best facilitated by MRI with and without contrast and include aneurysms, metastases (especially prostate), lymphoma, pituitary tumors, chordomas, primary bone tumors, acoustic neuromas, esthesioneuroblastomas and even gliomas.

A modality which may prove to be of more prognostic than diagnostic use is PET scanning. DiChiro [62] has reported the results of PET in 17 tumors showing that the metabolic activity of recurrent tumors was higher than that of non-recurrent tumors. The use of such information in a prospective manner is yet to be reported.

The diagnostic information required for preoperative planning is usually adequate from the CT and MR appearance. The addition of MRA or MRV to assess sinus patency or occluded segments is useful for selected tumors. Tumor-vessel relationships may be easier to characterize on MRI than angiography.

Surgical considerations

Surgical adjuncts

Embolization

Because of the often vascular nature of meningiomas of the skull base, embolization has gained popularity as a preoperative adjunct (Fig. 1). Embolization serves not only to devascularize the tumor and produce less blood loss during resection, but may also soften the tissue as it necroses and thereby facilitate removal with such instruments as the ultrasonic aspirator. It is particularly useful for patients with very vascular lesions, elderly patients unable to tolerate significant blood loss, or patients with religious objections to transfusion.

Embolization requires experience and knowledge of the typical patterns of vascular supply to lesions in various locations in order to fully appreciate vascularity and avoid embolization through potentially hazardous anastomoses, especially around the skull base where internal to external carotid anastomoses may be extensive [63–65]. Operation is usually performed three to five days after the procedure, although optimal timing may depend upon the embolic material used [64, 66]. Com-

plications may also be related to choice of embolic material [67]. Most series report at least qualitatively that basal tumors tend to be less vascular than those at the convexities, making these locations perhaps less likely candidates for embolization [63, 68]. In Teasdale's series [68] of 26 external carotid embolizations, complete obliteration of the tumor circulation was achieved in 23 of 26 cases, and felt to be 85–90% reduced in the remaining three. Surgery was felt to have been facilitated in about 50% of the cases, mostly in those tumors that had predominantly external carotid supply. Pathological examination revealed infarction in 14 of 26 tumors. In Richter's series [66], surgery was felt to be easier in 29 of 31 cases following embolization, although there was no benefit if the tumor was dominantly supplied by internal carotid branches. Blood loss was not quantitated in these series.

Balloon occlusion test and carotid bypass

Temporary balloon occlusion of the carotid artery, often performed in conjunction with cerebral blood flow studies, has become a popular test for the evaluation of vascular reserve for lesions such as cavernous sinus tumors where the carotid artery is at significant risk of injury during surgical removal [56, 69] (Fig. 2). Occlusion of the internal carotid artery for 10–15 minutes identifies patients with varying degrees of risk should they require temporary or permanent internal carotid artery occlusion. This information is useful for anticipating the use of adjuncts such as intraoperative hemodynamic or anesthetic techniques of cerebral protection, or possible vascular bypass. Dolenc has expanded on descriptions of the surgical anatomy of the cavernous and petrous carotid artery and the techniques of intracranial bypass relevant to resection of tumors which may involve the cavernous carotid [70, 71]. Sekhar [72] has reported on the use of temporary balloon occlusion/cerebral blood flow studies in five patients who eventually required internal carotid artery bypass during meningioma resection. No patient was a candidate for STA-MCA bypass. One patient failed the temporary balloon occlusion while four others had no clinical changes but did have blood flow reduction. All but one of the patients who had cerebral blood flow reduction had

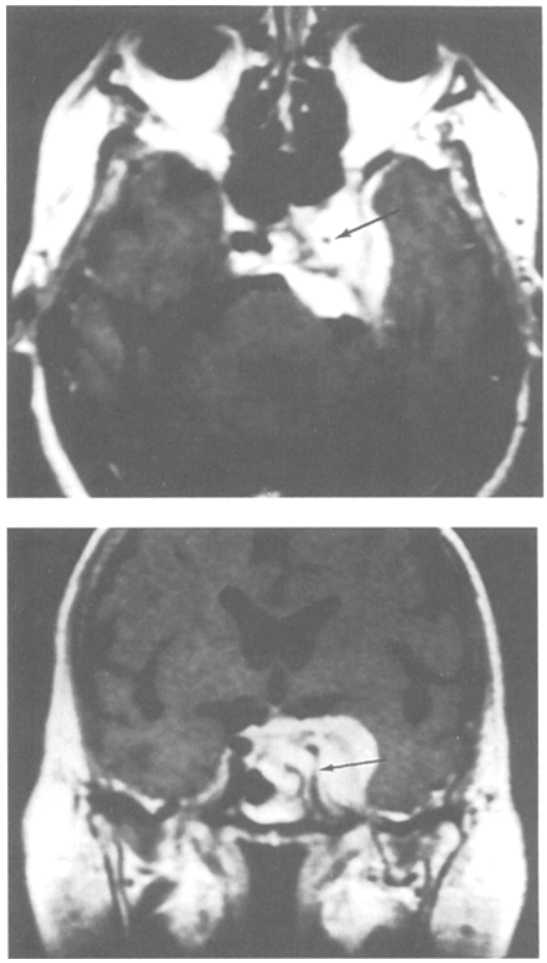


Fig. 2. Axial (A) and coronal (B) gadolinium enhanced MRI of a meningioma involving the cavernous sinus. The carotid artery has been narrowed by the tumor (arrow).

new transient deficits postoperatively, with occlusion times from 1 1/2 to 5 hours. The patient who failed the temporary balloon occlusion clinically had later evidence of border zone infarction on CT scan. Balloon occlusion testing may itself incur morbidity, and such tests are not entirely benign [76]. Additionally, the relative merits and indications for these adjuncts have not been conclusively demonstrated in terms of improved neurological outcome for these patients [76], nor has there been sufficient long term follow up of these extensively resected tumors to demonstrate the benefit of such measures at the present time. Since the ability to avoid neurologic injury with this type of testing is not clear from these results, the demonstrated safe-

ty of STA-MCA bypass where applicable has been emphasized.

Additionally, Spetzler and Fukushima [73] have reported the results of petrous to internal carotid artery bypass in 18 patients, most with cavernous aneurysms. No special studies were performed to select these patients. Two grafts occluded, one asymptomatically, and one which was repaired intraoperatively. Complications included one stroke, one temporary hemiparesis, one transient increased third nerve palsy, and one case of decreased hearing from eustachian tube injury during petrous exposure. Other technical notes regarding these procedures have appeared recently including use of an intraluminal shunt during bypass to prevent ischemic complications [74, 75].

Intraoperative monitoring

Intraoperative monitoring of neurologic function has been increasing in use as an adjunct to reduce surgical morbidity for skull base tumors. The variety of monitoring techniques available include scalp EEG, visual evoked responses, somatosensory evoked potentials, brainstem auditory evoked responses, and cranial nerve monitoring [77]. Facial nerve monitoring for acoustic neuroma surgery has been of proven benefit in preserving function of the nerve [78] and has served as the basis for encouraging monitoring of other cranial nerves particularly in the cavernous sinus region. Sekiya [79] has reported on such techniques to assess function and locate electrically the IIIrd, IVth, and VIth nerves in patients undergoing skull base surgery. Significant technical difficulties exist, and the benefits of monitoring in terms of preservation of function have not yet been demonstrated. Visual identification of these nerves may be more feasible for experienced surgeons in these cases [79].

Pulmonary embolus

The risk of pulmonary embolus in neurosurgical patients after craniotomy for brain tumors of all types is about 1% [80, 81]. This risk has been reported to be higher in patients with meningiomas compared to other types of brain tumors [82], however, it may be more related to independent risk factors such as length of operation or neurologic disability than histopathology [80, 83, 84]. Whether pathology reflects thrombogenic potential has not yet been settled [80, 85]. Al-Mefty has reported a pulmonary embolus rate of 38% in his series of patients with petroclival meningiomas, and this complication is frequently noted in the morbidity and mortality of most skull base series. Prophylaxis and treatment are vitally important issues [81], particularly for patients with skull base tumors where lengthy surgical procedures are common.

Natural history

Management decisions for these lesions must consider their natural history in relation to the risks and benefits of surgery or other treatment modalities. Surgical resection remains the mainstay of definitive therapy, but the goals of therapeutic intervention or conservative management must be individualized for each patient. The use of hormonal or other chemotherapy is being investigated but currently cannot be considered for other than exceptional circumstances in research protocols.

The natural history of the vast majority of these tumors is one of slow growth. Incidentally discovered tumors have increased with the development and widespread usage of modern neuroradiological techniques, providing an opportunity to follow the natural history of these tumors [86]. The number of these tumors which might become symptomatic is not known for certain, but has been estimated to be as low as 1% [87], a finding supported by the frequency of incidental tumors at autopsy.

There are few reports of the natural history of meningiomas followed radiographically. Duma cites a report by Goodman [88], who observed a series of 24 patients with skull base tumors with variable follow-up from 2 to 18 years after the onset of symptoms, finding growth in only three cases. Sekhar [69] followed seven cavernous sinus tumors for an average of 25 months and demonstrated growth in only one case (and regression in another). A later update reported progression in five of twelve cases, however the follow up period and radiographic

findings were not given [56]. Firsching [89] has reported an annual growth rate of 0.5–21% based on 17 tumors followed radiographically in a retrospective study with a median follow up of 21 months.

Since most tumors grow with time, management decisions must take into account a patient's age and estimated life expectancy. In the elderly, where the incidence of meningiomas is increased and the operative risk is greater, management decisions are especially difficult. Papo [86] reported 55% mortality in his series of 33 patients over 65 years of age undergoing tumor removal. More recent series report perioperative mortality rates ranging from 8 to 23% for patients over 70 [86, 90, 91]. Awad [91] found that 36% of these elderly patients were clinically worse three months after surgery. Since patients fare better if operated on before they are compromised by the tumor [90], surgical intervention is recommended before the progression of neurological symptoms to achieve optimal results [91]. As mentioned earlier, the clinical validation of additional techniques in the future, including bromodeoxyuridine labelling index, flow cytometry, PET scans and others may add to the knowledge of the natural progression of these tumors and improved predictive capabilities for the physician treating these patients.

Factors influencing recurrence

Most information about the natural history of meningiomas is derived from followup information on recurrence following partial resection. Recurrence rates are usually based upon mean follow up times, thereby probably underestimating these rates by including patients with short follow up. Variations in the reported rates of recurrences may reflect the lack of uniform methodology used, which in some reports did not use radiographic criteria as the means of diagnosis. Recurrence in the case of gross totally resected lesions can be partly explained by the finding of tumor rests in the surrounding dura at distances up to three centimeters away from the tumor margin [92].

Mirimanoff [10] studied the results for recurrence in 225 patients treated from 1962 to 1980 using life-table analysis. Recurrence rates following total removal were 7%, 20%, and 32% at 5, 10, and 15 years respectively, while the rates following subtotal removal were 37%, 55%, and 91% for the same intervals. Certain tumor locations, including basal, were associated with a lower rate of complete removal and corresponding increased recurrence rates. Sphenoid ridge tumors were notable in that only 28% were totally resected, resulting in a relapse rate of 34% at five years. Studies with longer follow up may more accurately reflect the actual growth rate of meningiomas. Jaaskelainen [13] reported on 657 patients including 69 followed for more than 20 years, and found a 20 year recurrence rate of 18% following total resection and coagulation of the dural base.

Extent of resection, regardless of other considerations, remains the most important factor influencing recurrence. This is particularly relevant for skull base tumors where it may be considerably more difficult to remove involved dura or bone. Simpson [93] originally described a grading system for assessing the degree of resection and correlated it with recurrence. A recurrence rate of 9% at 10 yrs was found after Grade I removal, defined as resection of all gross tumor as well as all dural attachments and any involved bone. Histology also plays a role, and patients with tumors which are WHO Grade I, Grade II, and Grade III recur at rates of 3%, 38%, 78% respectively at five years [9]. It has also been noted that second recurrences occur with a shorter disease free interval [12].

In terms of survival, Kallio [9] has reported a series of 935 patients with long term follow up largely predating the CT era. The survival rates for these patients were 82.5% at five years and 62.6% at 15 years. The relative survival rate in comparison to the expected survival for the cohort was 77.9% at 15 years. Patients with subtotal removal lost 36% of their expected remaining life; those with total removal lost only 5%. This information emphasizes the benefits of complete resection as the initial treatment whenever possible.

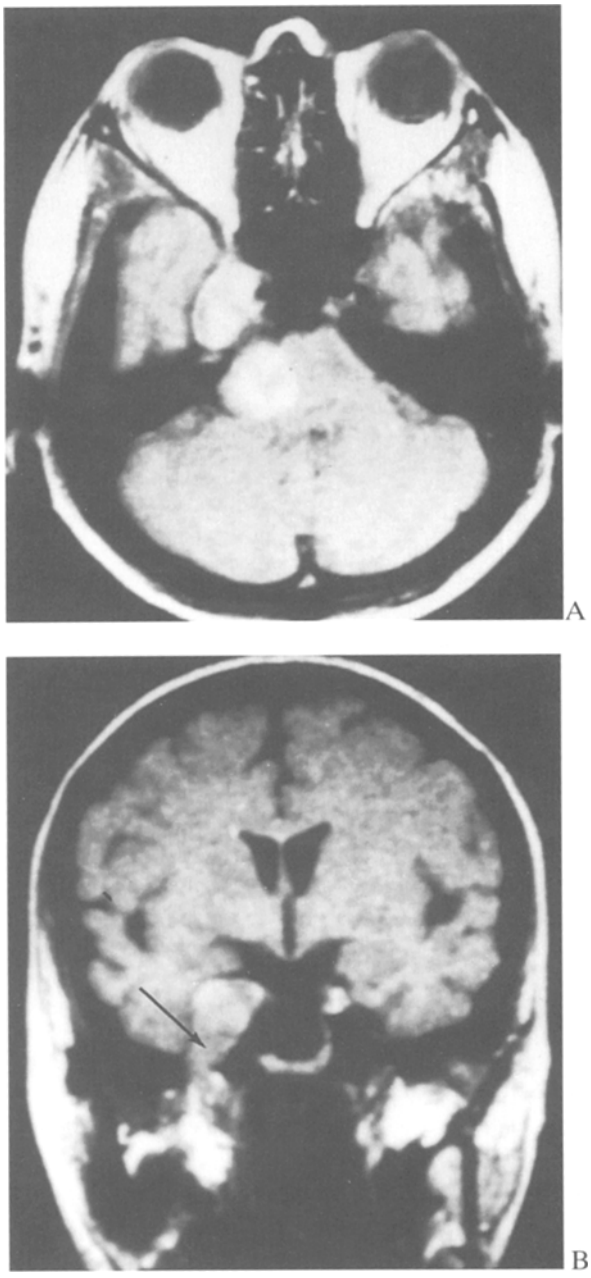


Fig. 3. Axial MRI (A) of a Meckel's cave meningioma. The coronal MRI (B) shows the tumor extending through the foramen ovale (arrow). This tumor was removed through a frontotemporal craniotomy combined with an orbitozygomatic osteotomy.

Operative approaches

Improved outcome for patients with skull base meningiomas has been facilitated by advances made in surgical approaches. A better understanding of skull base anatomy has led to the development of approaches predicated on increasing surgical exposure by preferentially removing portions of the skull rather than relying on brain retraction. The evolution of skull base teams comprised of neurosurgeons, plastic and reconstructive surgeons, head and neck surgeons, otolaryngologists and ophthalmologists has united several surgical disciplines, facilitating a more cohesive approach to the components of skull base surgery which encompass exposure, tumor removal, and subsequent reconstruction. Although many variations of skull base approaches exist, this section will highlight some of the particularly helpful basic approaches which have been developed in recent years.

Extended frontal approach

The extended frontal approach evolved from the transbasal approaches first popularized by Derome [94]. This approach combines a bifrontal craniotomy with an orbitofrontoethmoidal osteotomy to minimize frontal lobe retraction [95]. By removal of the orbital rims and opening into the ethmoid sinus, there is excellent exposure of tumors evolving from the anterior skull base and extending into the nasal sinuses. This exposure, often in combination with a transfacial approach, is particulary useful for en bloc resection of malignant lesions. Lesions located in the upper and middle clivus or extending into the sphenoid sinus can be resected. The wider exposure also reduces CSF leak by facilitating reconstruction through use of a pericranial flap which can be left vascularized and sutured to the dura posterior to the margins of bony removal. Exposure is limited by the optic nerves, cavernous sinus and petrous apices. Both olfactory nerves are sacrificed. This approach is useful for subfrontal meningiomas, particularly with nasal extension, esthesioneuroblastoma, malignant tumors of the nasal sinuses, fibrous dysplasia, and repair of complicated CSF leaks. For most anterior cranial pathology, however, this extensive exposure is not necessary and a simple bifrontal craniotomy will suffice.

Fronto-temporal craniotomy with orbitozygomatic osteotomy

This approach is an extension of the pterional ap-

proach which has historically been one of the most versatile for providing access to skull base lesions and the circle of Willis. A frontotemporal craniotomy is followed by orbitozygomatic osteotomy with removal of the orbital rim and zygoma as a separate piece [69, 96] (Fig. 1). The sphenoid wing is removed along with portions of the orbital roof and the anterior clinoid process. This provides excellent exposure for tumors involving the cavernous sinus and upper/middle clivus. Considerably less temporal lobe retraction is required and early devascularization of tumors by interruption of their dural blood supply is facilitated. By splitting the sylvian fissure, the petrous apex region may be safely exposed (Fig. 3). Advances in understanding the anatomy of the cavernous sinus by individuals such as Sekhar [97], Parkinson [98], Dolenc [70] and Al-Mefty [99] has resulted in safe and successful removal of tumors within the cavernous sinus itself, an area once considered inaccessible. This technique is often combined with exposure of the carotid artery within the petrous bone to control its blood flow and to facilitate its repair or bypass if necessary. The morbidity from cavernous surgery is still more closely correlated to working within the cavernous sinus, rather than from the orbitozygomatic osteotomy and exposure.

Infratemporal approaches

Tumors involving the middle and posterior skull base, particularly along the petrous apex and clivus, can often benefit from the extending the infratemporal approaches. Fisch [100] pioneered this approach which was later modified and improved by Sekhar *et al.* [101]. A frontotemporal craniotomy is performed with division of the zygomatic arch. The mandibular condyle is resected and portions of the temporal bone are removed to gain exposure of the petrous portion of the carotid artery which is then mobilized to allow removal of the petrous apex. This is particularly suitable for petrous apex meningiomas that extend further caudally into the clivus. This approach has the advantage of exposing tumors in the middle to lower clivus with minimal brain retraction. Cranial nerve injury is minimized by working medial to cranial nerves VII through XII rather than lateral as in standard posterolateral approaches. The approach is limiting for tumors extending into the ipsilateral cerebellopontine angle and inferiorly down to the foramen magnum and has the disadvantages of sacrifice of the ipsilateral eustachian tube (ultimately necessitating tympanostomy). Potential risks include injury to the internal carotid artery, facial nerve or cochlea within the temporal bone.

Combined subtemporal craniotomy and presigmoid transpetrous approach

There are a variety of approaches that require partial resection of the petrous bone to gain exposure. Typically, subtemporal craniotomies or retrosigmoid approaches were used for tumors in the petroclival region. The presigmoid approach involves the combined use of a temporal craniotomy with a posterior fossa craniectomy which has been modified by drilling out the mastoid and the posterior portion of the petrous bone with preservation of the facial and hearing structures [102]. By exposing the posterior fossa dura anterior to the sigmoid sinus, a dural opening can be made extending from the jugular bulb to the superior petrosal sinus where it can be connected to a posterior temporal dural opening by dividing the tentorium. The sigmoid sinus and all neuro-otological structures are preserved while providing exposure of the petroclival region. This approach improves on other transtentorial approaches by minimizing retraction of the temporal lobe and cerebellum and brings the operative site closer with a more lateral approach that better visualizes the brain stem-tumor interface. Petroclival tumors that are slightly lateral from the midline are well-suited for this approach however midline upper clivus tumors are often better approached from an infratemporal approach since the nerve roots are less stretched by the tumor and therefore more prone to injury. Exposure of the lower clivus often requires a simultaneous retrosigmoid approach. Some posterior temporal lobe retraction may still be required which is a disadvantage but usually the vein of Labbé can be preserved and retracted along with the tentorium to preserve its junction with the sigmoid sinus.

Extreme lateral transcondylar approach to the foramen magnum

The extreme lateral approach provides wide exposure for tumors in the ventrolateral portion of the foramen magnum and lower clivus [103]. It involves a retrosigmoid craniectomy and C1 laminectomy with mobilization of the vertebral artery from the vertebral canal. The occipital condyle is partially drilled away permitting a very lateral approach. Brainstem retraction is minimized compared to standard posterior suboccipital craniectomies. The extreme lateral approach permits direct visualization of the interface between the tumor and the lower brain stem. Minimal brain or spinal cord retraction is required and spinal stability is not compromised.

Surgical management and results

Surgical resection is the treatment of choice for most skull base meningiomas. The aggressiveness of resection may be affected by the operative risk and clinical condition of the individual patient, but for the majority, complete resection including a dural margin and any involved bone should be the goal to minimize recurrences. A better appreciation of surgical anatomy combined with advances in the development of approaches to the skull base have facilitated this important goal. Although promising, the results of extensive resections have not had sufficient length of follow up to assess their benefit. Tumor size, location, involvement of vital structures, and other features create a significant diversity in outcome, which must be considered when evaluating risk-benefit ratios.

Anatomically, skull base meningiomas may extend from one cranial fossa to the next and frequently involve more than one important anatomic area. Certain locations bear characteristic clinical features affecting management and outcome including olfactory groove/subfrontal, parasellar and medial sphenoid wing, cavernous sinus, petroclival, cerebellopontine angle, and the foramen magnum.

Olfactory groove meningiomas

Olfactory groove tumors are often slowly progressive and may reach considerable size before detected. Bakay reported an average tumor size of 6.1 by 4.5 cm in 36 patients [104]. Clinically, the predominant presenting symptoms are visual changes in about one half of the cases and cognitive changes in one-third. Anosmia is also frequently noted, though it is less commonly the cause for presentation [105]. Anatomically the tumors arise from the cribriform plate and ethmoidal dura near the spheno-ethmoidal suture. Blood supply is via ethmoidal branches of the ophthalmic and anterior branches of the middle meningeal artery. The surgical approach is usually through a bifrontal craniotomy, though a pterional approach has also been used [105]. Involved bone can be removed and the dural defect repaired with pericranium following tumor removal. If extension through the ethmoid bone is significant the risk of cerebrospinal fluid leak is increased, and additional measures such as fascial or bone grafts are often used to reconstruct the skull base. Outcome has improved with modern neurosurgical technique. Solero [106] reported 98 patients treated between 1947 and 1977 with 92 total removals, 17 deaths and three recurrences. Symon [107] in 1977 had 18 complete removals with no mortality. Ojemann [108] reported one death due to pulmonary embolus out of 17 patients all of whom had a complete tumor removal. Improvement in visual acuity and visual field can be expected, even when severe, longstanding deficits are present [109].

Parasellar meningiomas

Tumors of the parasellar region include those classified as clinoidal, planum, diaphragma, or tuberculum sellae meningiomas, and may include other extensive tumors of the medial sphenoid wing. Growth into the optic foramen may result in visual compromise, although most visual disturbance is related to compression of the optic chiasm. Tumors limited to the tuberculum sellae may have a relatively small dural attachment in comparison to their overall size, making thorough removal easier in

some cases (Fig. 4). Visual outcome has been reported to be better in these cases [110]. These tumors may be difficult to differentiate preoperatively as arising from any particular area of the dura of the parasellar region [111] though the use of MRI may improve this capability. Anatomic features which may not be apparent until operation can have a significant bearing on outcome. Al-Mefty [112] has described three groups of tumors arising from the anterior clinoid based on anatomic features, and related them to presentation as well as operative difficulty because of the presence or absence of arachnoid planes between tumor and vital structures such as the cavernous and supraclinoid carotid or the optic nerves. Diaphragma tumors may grow retrochiasmatically causing pituitary dysfunction. Most often, the clinical history of these suprasellar lesions is one of asymmetric visual loss, which occurs in almost all patients [113, 114]. Other findings include headache, mental changes, or anosmia, and occasionally pituitary or hypothalamic dysfunction as well.

As with many meningiomas, interruption of blood supply is generally desired early in the course of the operation [111]. Tumors of this region, particularly the tuberculum, are fed by the posterior ethmoidal branches of the ophthalmic arteries with frequent contributions from anterior cerebral, middle cerebral, or middle meningeal artery branches. Embolization is often hazardous [63, 111] due to the primarily internal carotid supply. Differentiating perforators from tumor feeders is important during surgical resection. The most popular operative approaches include bifrontal, pterional or orbitofrontal craniotomies. A less favorable outcome may be anticipated in large tumors, particularly those greater than three centimeters in diameter as noted by Cushing [3] and confirmed by others [111, 113]. Duration of symptoms may also affect outcome, as Symon [114] has noted a more favorable prognosis when symptoms are present for less than two years. As mentioned above, the anatomic location may also relate to outcome, with purely tubercular meningioma patients faring better than those with a more extensive dural base. Surgery has been successful in improving vision in the majority of cases, with most series reporting improvement in two-thirds of patients having preoperative visual compromise. Outcome correlates with several factors including duration of symptoms, preoperative visual condition, tumor size and location and uni- or bilaterality of optic nerve involvement [114]. Occasionally dramatic results can be obtained: one patient in the series of Gregorius [109] with finger-counting vision of six years duration improved to 20/40 after tumor removal, and two patients of Al-Mefty had recovery of vision in a totally blind eye [35]. Complications and mortality, though very significant in the past, have been reduced in more recent series utilizing microsurgical techniques [113]. Overall, visual deterioration occurs in 3 to 24% of operated cases [35, 109, 111, 114]. Pulmonary embolus is a frequent complication following surgery [111] with various factors contributing to this cause of death. Tumors located in a suprasellar location have been associated with increased thromboembolic risk [115], compared to

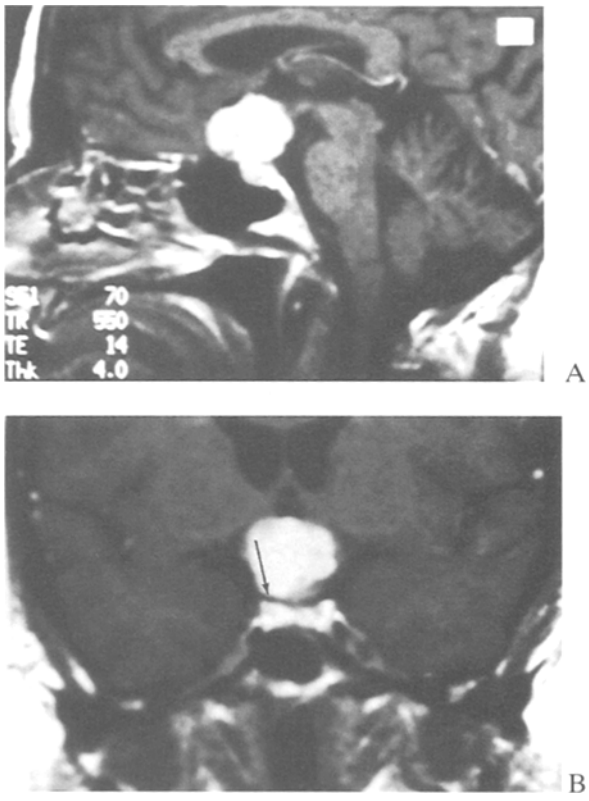


Fig. 4. Sagittal (A) MRI of a tuberculum sella meningioma. The sella is not enlarged. Coronal (B) MRI demonstrates intact diaphragma sella (arrow) separating tumor from the pituitary gland.

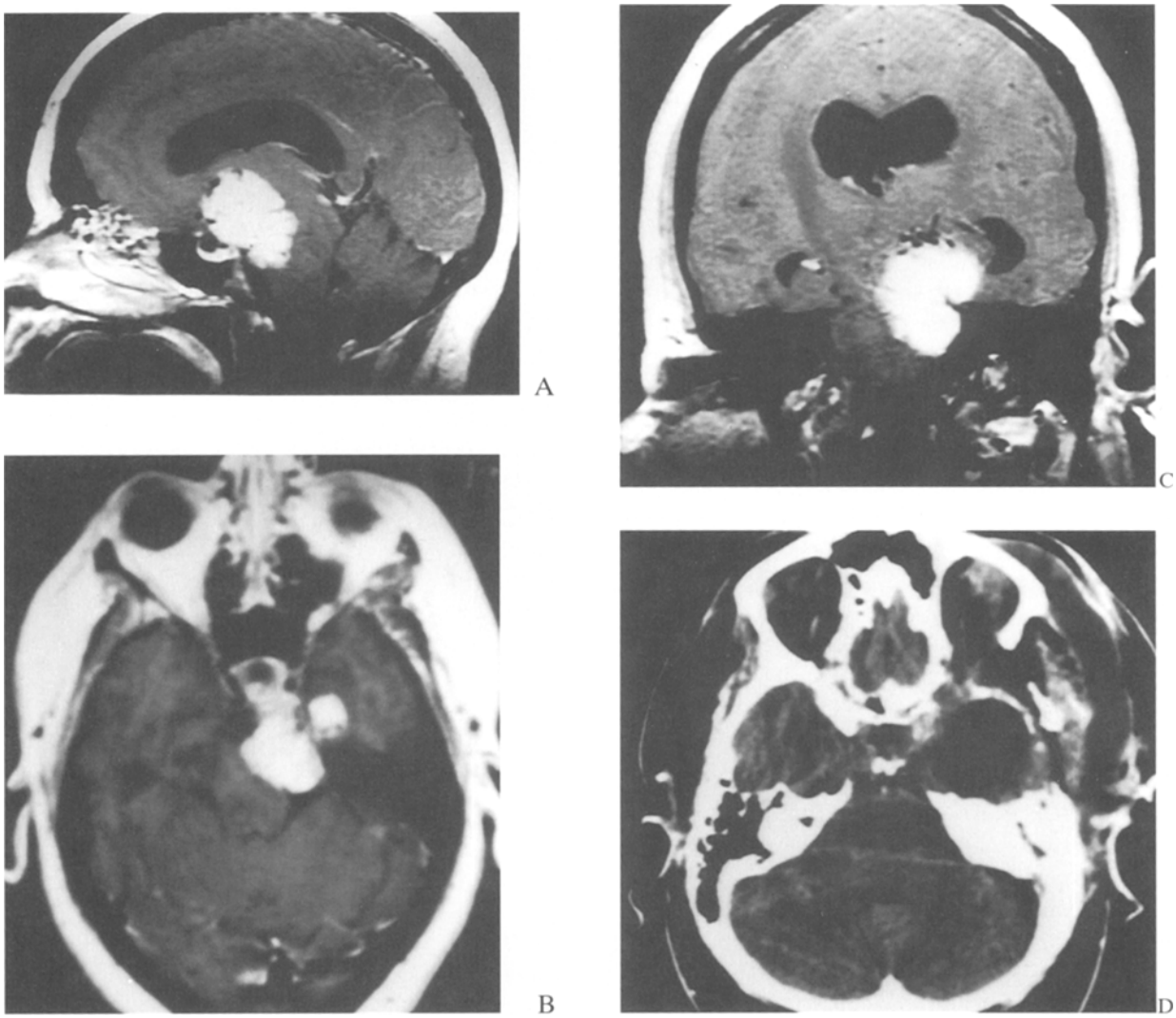


Fig. 5. Sagittal (A), axial (B) and coronal (C) gadolinium enhanced MRI of an extensive meningioma petrous apex involving the cavernous sinus and compressing the third ventricle causing hydrocephalus. The tumor was completely removed in two stages through a frontotemporal craniotomy combined with an orbitozygomatic osteotomy. Postoperative CT scan (D) demonstrates tumor removal.

other locations. This complication might be reduced by preoperative screening in selected patients as well as through routine use of prophylaxis [81].

Cavernous sinus meningiomas

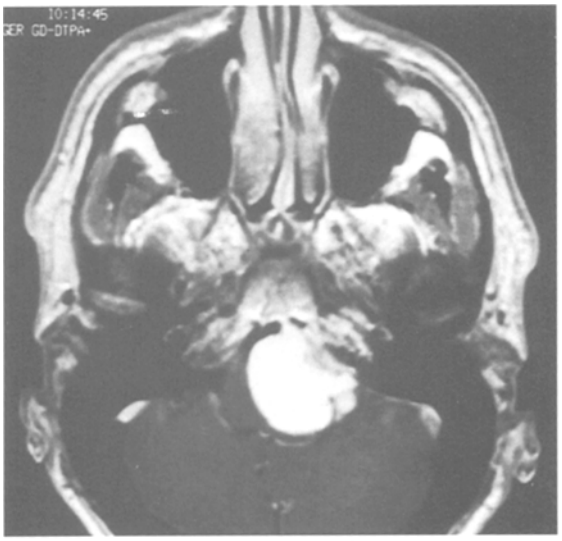
Tumors involving the cavernous sinus present a formidable surgical obstacle which has only recently been successfully challenged. Meningiomas make up about 40% of the tumors found in this area [71] and may arise from the arachnoid network of the sinus itself or secondarily involve the cavernous sinus by extension from other areas. There has been considerable recent interest in understanding cavernous sinus anatomy and improving the surgical approaches to these lesions, so that resection of these benign tumors, even in difficult cases, is now possible. As an alternative, certain patients with orbital extension of cavernous sinus tumors and unacceptable surgical risk may have histological confirmation through an orbital percutaneous needle biopsy [116]. Stereotactic irradiation has been used

as a therapeutic modality in selected cases though long term follow up is lacking [88].

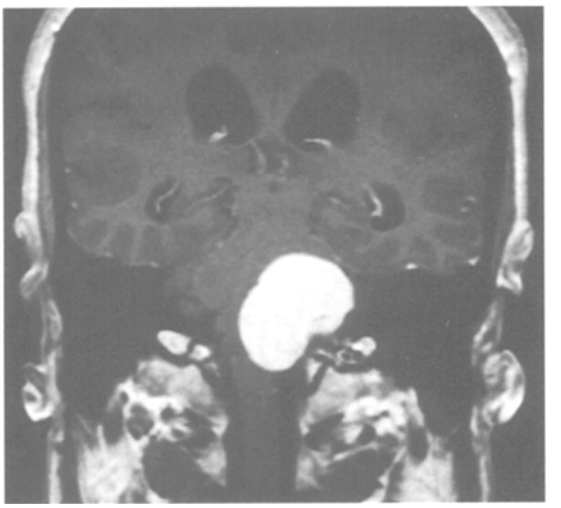
The tumor's relationship to the cavernous sinus, which has been described as a pentahedron with superior, inferior, lateral, medial, and posterior walls, is important in selecting one of several surgical approaches [56, 69, 97]. Tumor blood supply is usually from the middle meningeal artery, cavernous internal carotid branches and branches of the ophthalmic artery. Tumor removal may be hindered by encasement and narrowing one or both internal carotid arteries, as well as involvement of multiple cranial nerves, especially, II, III, IV, V_1, and VI (Fig. 2). Interdural tumors between the dura propria and membranous dura, or minimally invasive tumors may be easier to resect [117]. The approach may be intra- or extradural, with an orbitozygomatic approach most preferred, although various combinations of pterional, transpetrosal and transzygomatic approaches can be useful [56, 69, 71] (Fig. 1), depending on the exact tumor location. Common presenting symptoms include headache, extraocular palsies, trigeminal symptoms such as neuralgia, visual difficulties, or exophthalmos. Dolenc has reported a large series of 63 tumors of the cavernous sinus including 40 benign and 2 malignant meningiomas [71]. Data on the meningiomas were not given separately from the other tumors although they were notably more difficult to treat. Four patients in the series died – their pathological diagnoses were not given. Permanent deficits of the third through sixth cranial nerves were limited to twelve patients, though about half had transient cranial nerve palsies. Two patients each suffered injuries to the optic nerve and internal carotid artery. Removal was complete in 45 of 63 patients, with incomplete resection due to internal carotid artery infiltration in nine patients, malignancy in two patients, and cranial nerve infiltration and postoperative scarring in seven patients. Patients had preoperative angiograms without embolization, and intraoperative monitoring and brain protection were not used. The duration of follow up and recurrence in the meningioma group was not stated.

Sekhar [69] has reported on one malignant and sixteen benign meningiomas of the cavernous sinus. To achieve complete tumor resection, planning for possible sacrifice of the internal carotid artery was done by preoperative balloon occlusion testing with cerebral blood flow studies. Intraoperative cranial nerve monitoring was also used to assist in identification and preservation of these nerves during surgery. This group achieved total removal in 13 of 17 patients. The permanent cranial nerve outcome (excluding those expected from surgical approach, such as anosmia) included one optic nerve worsening, four fourth nerve palsies, three V_1 palsies, and four fourth nerve palsies. Most patients maintained their preoperative status: six of sixteen patients with fair or poor extraocular movements preoperatively improved dramatically and one optic nerve improved as well. One meningioma recurred after subtotal removal, and was reoperated followed by irradiation of the residual. A later update of Sekhar's series [56] with 45 meningiomas involving the cavernous sinus reported complete excision in 37 cases. Half of the patients had a minimum of one year of followup. Recurrence occurred in one of the totally resected cases, while three tumors regrew in the subtotally resected group.

Sekhar's original study included some important insights into the natural history of nonoperated tumors and unexpected pathological results. Of seven nonoperated meningiomas followed radiographically for an average of 25 months, four were unchanged, one grew dramatically, and one even regressed spontaneously (worsened symptoms during pregnancy with resolution following delivery). In addition, six patients operated on in the series had unexpected pathology: two meningiomas were misdiagnosed preoperatively as a malignant tumor and a schwannoma, and two tumors misdiagnosed as meningiomas turned out to be a plasmacytoma and a hemangioma at surgery. The implications for irradiating unbiopsied lesions and the potential findings on short term radiographic follow up may be very important [88], particularly since the results of radiosurgical series have limited followup and often lack confirmation of tumor histology [24]. Coffey [24], in reporting excellent results of treatment of meningeal hemangiopericytomas with gamma knife radiotherapy, has questioned earlier reports of rapid tumor regression following radiosurgery for presumed meningiomas which were not verified



A



B

Fig. 6. Axial (A) and coronal (B) MRI of a cerebellopontine angle meningioma demonstrating significant brainstem compression. This tumor was removed through a standard retrosigmoid suboccipital approach.

pathologically. The dramatic shrinkage of some of these tumors suggests that they were actually hemangiopericytomas. Tissue diagnosis is strongly recommended in all patients prior to undergoing any form of therapeutic intervention.

Petroclival meningiomas

Meningiomas of the petroclival region were historically considered inoperable and continue to be among the most challenging of lesions (Fig. 5). Progression of lower cranial nerve dysfunction, brainstem or cerebellar compression, and hydrocephalus, can contribute to clinical deterioration. Patients most often present with headache, gait ataxia, diplopia, facial pain or numbness, hearing loss and other posterior fossa symptoms [118–125]. Blood supply is usually from internal carotid artery branches as well as branches of the middle meningeal and ascending pharyngeal arteries. Angiography has been useful in assessing basilar artery encasement or narrowing, and patency of the venous sinuses, although MRA may eventually supplant this procedure. The importance of anatomic location medial to the trigeminal ganglion and above the lower portion of the clivus has been emphasized [118–123], differentiating them from cerebellopontine angle and foramen magnum tumors and impacting on the choice of optimal surgical approach. Tumors of Meckel's cave have also been included with these tumors, though they have salient clinical differences [124–126]. Surgical considerations of any approach include: degree of exposure, especially of medial structures; necessity for ligation of dural sinuses or compression of veins such as Labbé; amount of brain retraction required; possible sacrifice of hearing or other cranial nerve function; and necessity of operating between the cranial nerves or around them. Factors contributing to surgical difficulties include extension to the cavernous sinus or across the midline [121], firm tumor consistency, pial adherence, and encasement of the cranial nerves and blood vessels [120]. Modern reports utilizing skull base techniques demonstrate a total removal rate of 75–84%, without perioperative mortality. This contrasts historically with the lone report of a total removal prior to 1970, and prohibitively high intra- and perioperative mortality rates [127]. Major morbidity can be significant, with frequent postoperative cranial neuropathies, however, many patients are improved over their preoperative condition and operative outcome must be assessed in view of the progressive deterioration associated with the natural history of these tumors. Most series considered outcome good in 50 to 60% of patients [118–123]. Bricolo [21] reports 30% of their patients surpassing their preoperative performance scores

with time, although mortality was higher compared to other recent reports.

Cerebellopontine angle meningiomas

Tumors of the cerebellopontine angle arise from the dura of the petrous bone with progressive growth into the cerebellopontine angle cistern where symptoms develop from involvement of Vth, VIIth, and VIIIth cranial nerves, the petrosal veins, anterior-inferior cerebellar artery, and the pons (Fig. 6). Meningiomas make up about 6–8% of the lesions in the cerebellopontine angle with acoustic neuromas far more common [128]. Contrast-enhanced MRI demonstrating a dural based homogeneously enhancing mass without extending into the porus acusticus is usually diagnostic. Presentation is often with gait ataxia or abnormal hearing (the high incidence of facial pain in the series of Sekhar and Janetta [129] is probably due to referral bias). Blood supply is through meningeal branches of the vertebral artery, the meningohypophyseal trunk and other petrous branches of the internal carotid artery, middle meningeal artery branches, and the ascending pharyngeal branch of the external carotid artery. A lateral retrosigmoid suboccipital craniectomy is the preferred surgical approach. Sekhar [129] reported 22 patients with no mortality and gross total removal in 14. Samii [128] noted several anatomic differences relevant to outcome. The relationship of the tumor anterior or posterior to the internal auditory canal had surgical implications as all 24 posterior tumors were completely removed, compared to 29 of 32 anterior tumors. Gait ataxia was more common in posterior tumors while hearing impairment predominated in anterior tumors. Yasargil has also reported excellent results in a large series of patients [130]. These reports demonstrate a better general outlook for these tumors as compared to nearby petroclival tumors.

Meningiomas of the foramen magnum

Tumors of the foramen magnum region have been classified as anterior/anterolateral (or craniospinal)

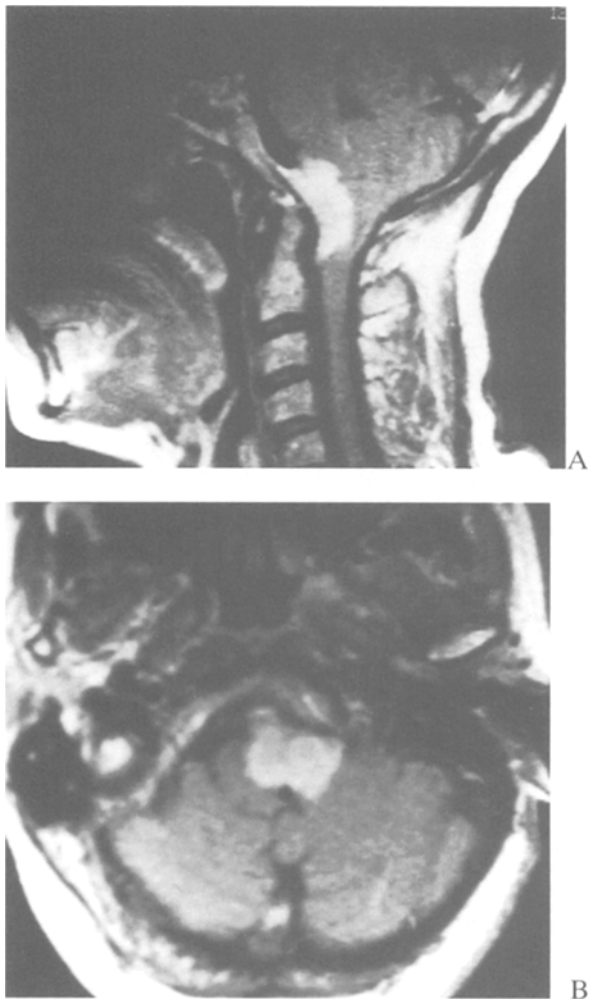


Fig. 7. Axial (A) and sagittal (B) gadolinium enhanced MRI of a foramen magnum meningioma. This tumor was resected through an extreme lateral transcondylar approach.

tumors and posterior/posterolateral (or spinocranial) tumors (Fig. 7). Stein [131] found these tumors to comprise 2.5% of a series of 1000 meningiomas which is corroborated in several series averaging a frequency of about 2% [130–132]. Meningiomas are the most common extradural lesion in this region. The classical clinical triad of head and neck ache, atrophy of the intrinsic hand muscles and progression of sensorimotor deficits from one arm to the other extremities, is often misdiagnosed as cervical spondylosis [131, 133, 134]. C1 and C2 sensory involvement is thought to be responsible for cervical pain. Intrinsic hand muscle atrophy, noted in up to 50% of cases [131], has been attributed to infarction

of the lower cervical cord on the basis of venous rather than arterial flow obstruction [135]. This atrophy may even involve the intercostal muscles. Cranial nerve involvement is most commonly of the XIth nerve [131, 136], with occasional deficits of other lower cranial nerves. The majority of tumors are of the anterior/anterolateral type. Blood supply is through the meningeal branches of the vertebral arteries, ascending pharyngeal arteries and occipital arteries. Surgical approaches have included suboccipital, lateral suboccipital, far-lateral, transcervical and transoral routes [131, 132, 136–140]. Operative mortality ranges from 5 to 30%, with good to excellent outcomes in 60–77% of cases [132, 136, 137, 140].

Adjuvant therapy

Radiation therapy

The role of radiation therapy for meningioma management has never been evaluated in a controlled prospective manner. Conventional wisdom holds that radiation therapy is generally not effective in treating slow growing, benign lesions because of the small population of cells actively dividing at any point in time, but this has been challenged by several clinicians. Current radiation modalities include external beam radiotherapy, linear accelerators, proton beam, gamma-knife, and interstitial brachytherapy, each of which has its proponents [141–145]. Recent reviews [145] suggest that the linear accelerator systems at present are the most cost effective and easily installed stereotactic devices. Use of these radiosurgical modalities has been increasing dramatically, and a growing number of reports of their use can be found, along with recommendations for more systematic evaluation of their risks and benefits [146].

Conventional fractionated radiation therapy

The use of radiation for malignant and angioblastic meningiomas has been effective in prolonging recurrence free survival in several reports, and must be differentiated from radiation therapy of more typical benign meningiomas. Chan [11] found an average survival of 5.1 years in 12 of 18 irradiated malignant meningiomas versus 7.2 months for non-irradiated lesions, though a treatment bias favoring the irradiated group may have existed. Adjuvant radiation treatment of meningeal hemangiopericytoma is also effective, reducing the five year recurrence from about 90% to 38% [24, 25, 147, 148]. These reports underscore the need to document histology prior to adjuvant therapy to assess the indications and avoid unnecessary risks.

Initial use of radiation therapy for meningiomas involved dosages in the range of 3000 to 4000 cGy, which were probably too low to demonstrate a clinical effect [12]. More recent fractionated dose plans utilize a range of 5000–6000 cGy. Many older series examining the effects of radiotherapy on meningiomas have compared unmatched retrospective results to recurrence rates in contemporary series, making interpretation difficult [93, 149, 150]. Unlike studies with malignant gliomas, none have used prospective methods with randomized controls.

Wara in 1975 reported results for meningioma patients treated with 5000–5500 cGy following partial resection [151]. The benefit of radiotherapy was reflected in recurrence rates of 29% (34 patients) in irradiated versus 74% (58 patients) in non-irradiated patients. Barbaro later updated these results in an often cited study [152]. Three groups of patients were reported; 51 patients had complete removal and a recurrence rate of 4% with average follow up of 78 months; 30 patients had subtotal removal alone with a subsequent recurrence rate of 60%; and 54 patients with subtotal removal and postoperative radiation therapy (avg 5253 cGy) had a recurrence rate of 32%. The authors stated that the groups were well matched by age, sex, and tumor location, and that a location bias favoring the non-irradiated group was present. Although the data is compelling, several flaws exist in this study. First, selection for irradiation was not systematic and inherent biases in this process may have been partly responsible for the difference in outcome. Other series have included poor clinical condition of the patient as a criteria for not giving radiation therapy, which would be expected to bias results in favor of patients receiving radiation therapy. Second, recurrence was defined as clinical progression rather

than by radiographic means or findings at reoperation. The possibility that radiation side effects were responsible for this progression was not discussed. Additionally, tumor location in the irradiated versus subtotal resection without radiation groups included more parasagittal tumors (27% versus 7%) in the former, and more posterior fossa tumors (17% versus 30%) in the latter, a bias which one might expect to favor the irradiated group. In general the flaws are those of any retrospective series antedating modern neuroimaging, and these data must therefore not be overinterpreted as indisputable evidence that radiation is beneficial.

Taylor [153] reported a similar retrospective series of 132 patients divided into three groups based on total resection, subtotal resection with radiotherapy, and subtotal resection only, with a shorter minimum follow up of two years. These patients were treated between 1964 and 1985 with recurrence documented by either angiography or CT. The 10-year actuarial local control rates reported were 18% for incomplete removal, 82% with the addition of radiation therapy, and 77% for total excision alone. Predicted actuarial survival at 10 years was 49% for the subtotal resection alone group versus 81% for the irradiated patients. Radiation therapy was only used in the latter part of the series after 1973, resulting in a shorter follow up bias in this group. Location distribution also differed substantially with more parasagittal (26% versus 0%) and falcine tumors (33% versus 0%) in the non-irradiated group. Sinus involvement was not mentioned, although this might affect recurrence rates, especially in older series.

Miralbell [154] has also reported a retrospective study matching subtotal resection cases with and without irradiation. The irradiated group had an 88% eight year radiographic progression-free survival compared to 48% in patients treated with surgery alone. The distribution of tumor locations was not given, and the irradiated group was significantly younger, though this was not independently associated with progression in the statistical analysis. Patients were selected for radiation by the individual physician's preference. Caution must be used in the interpretation of these data for the same reasons mentioned above. Though radiation probably has therapeutic benefit for selected tumors, better study design and long follow-up will be required to determine the specific indications.

Data for the effect of irradiation on recurrent tumors is sparse, and often limited to comparisons of disease free interval between first and second recurrence. Taylor's series [153] included 15 recurrences followed with surgery alone, and 10 who received radiation with or without radiation therapy. The local control rates were 30% and 89% respectively.

Radiosurgery

Stereotactic radiosurgical techniques and practice have expanded in recent years with continuously evolving indications for its use. Most series treating meningiomas have used either the gamma-knife or linear accelerators. Follow-up, even from the series of patients treated in Sweden where these techniques were first developed, are too short for meaningful interpretation. Steiner notes that only nine patients treated by his group have more than ten years of follow up [155]. The results of gamma-knife treatment of these lesions from various centers were summarized: Of 66 tumors in several series with follow up ranging from 1 month to 10 years, one tumor showed a decrease in size reported as significant, 18 tumors had 'slight' 'if any' decrease in size, 39 were unchanged, and 8 increased. The nine patients with long-term follow up were not presented independently. A separate anecdotal series of patients treated with a linear accelerator noted decrease in tumor size in one case of an angioblastic meningioma. The radiosensitivity of this histological variant is known to differ from that of benign meningiomas, stressing the importance of knowing the histology of the lesion being treated. The authors felt that attempted microsurgical removal of meningiomas should be the rule before contemplating radiosurgery.

Kondziolka [141] reported the use of gamma knife radiosurgery in 65 patients as either primary or adjuvant therapy over a 34 month period. Most of the lesions (88%) involved the skull base, including a large number of cavernous sinus tumors. No pathological diagnosis was obtained in 22 of these patients who were treated based on scan data alone.

No lesion was larger than 35 mm in diameter, or closer than 5 mm to the optic chiasm. The mean tumor margin dose was 17 Gy and was limited in some instances to avoid greater than 9 Gy to the optic structures. Patients were followed with CT or MRI at 3 months post-treatment, and then at 6 month intervals. Tumors decreased in size in 13 of 25 patients followed for longer than one year, and in 4 of 34 followed for less than one year, often associated with loss of central contrast enhancement. Two tumors increased in size. Pathology was not correlated to the radiographic or clinical course. Temporary neurological deficits occurred in three patients but responded to steroids, usually over many months. The short follow up, referral bias, poor quantitation of change in size, and lack of histologic diagnosis limit interpretation of this series.

Engenhart [144] reported the use of linear accelerator radiotherapy for seventeen patients with benign meningiomas of mostly basal locations, including six felt to be unresectable. Thirteen had prior surgery, and seven of these had recurrences. The mean single dose was 29 Gy, with an average field diameter of 40 mm, and matching of the 80% isodose contours to the tumor margin. Median follow up was 40 months. One patient died of a shunt malfunction, one from radionecrosis, and two of intercurrent illness giving a peri-treatment mortality of 24%. Eleven tumors were unchanged and two decreased in size as documented by CT and MRI. Nine patients had complications with neurologic worsening related to radiation. The authors recommended avoidance of single doses over 30 Gy or treatment volumes larger than 40 cm^3.

Duma *et al.* [88] reported the results of gamma knife treatment of cavernous sinus meningiomas in 34 patients with a median followup of slightly over two years. Seven tumors had no histologic diagnosis and indication for radiotherapy referral was not uniform. The median size of tumor treated was 21.5 mm, which is notable since smaller tumors are usually more amenable to surgical resection. The study found 56% of the tumors regressed on imaging studies and none grew during the period of study. 24% of patients had clinical improvement and 67% were unchanged. There was a 12% complication rate.

Risks of irradiation

The indications for use of radiotherapy must receive careful consideration, as there exists the potential for serious adverse side effects. Early-delayed reactions, usually transient, must be differentiated from late-delayed reactions which may take years to manifest and progress, sometimes with fatal consequences [156]. Al Mefty [157] reported the adverse sequelae of radiotherapy in 58 patients treated for benign pathology. These patients received a mean dose of approximately 5000 cGy, and were followed for an average of 8 years. 22 patients had 'complications', although this includes 17 cases with predominantly radiographic signs of brain necrosis. Overall, clinically relevant complications attributed to irradiation occurred in 19% including two patients with visual deterioration, six with pituitary dysfunction, two with marked organic brain syndrome and brain necrosis, and one with a radiation-induced clival meningioma.

In summary, though the findings of clinical improvement and radiographic regression in series utilizing radiation therapy are encouraging, comparison with surgical series will require longer follow up and better organized trials. Results of stereotactic radiotherapy suffer from short follow up, non-systematic indications for treatment, and inclusion of tumors without histological diagnosis. The results for external beam therapy are derived from retrospective series, and though often quoted as clear evidence of the benefits of radiation, must be accepted as uncontrolled, non-prospective data. Since the potential negative side effects of radiotherapy are considerable, serious consideration must be given to its indications and use.

Summary

Advances in skull base microsurgical techniques combined with improvements in radiographic imaging, postoperative management and rehabilitation, and interventional radiology have led to improvements in outcome for patients with cranial base meningiomas. Management decisions for patients with these tumors can be complex and should be individualized to the patient. These decisions are

influenced by many factors including potential surgical morbidity, likelihood of adequate tumor resection, presence of neurological deficits, patient's age and medical condition, natural history of meningiomas, and possible therapeutic alternatives. Various means of prognosticating the growth potential of a given tumor are being investigated, though none have yet been confirmed for their predictive value in typical, histologically benign meningiomas. Completeness of resection is the major prognostic factor determining the outcome of patients with meningiomas in terms of length of survival, risk of recurrence, and neurological disability. Fractionated radiation and stereotactic radiosurgery can be useful for specific tumors, however the indications for their usage are still controversial and await further follow up.

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