Cavernous Sinus Meningioma with Orbital Involvement: Algorithmic Decision-Making and Treatment Strategy

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Abstract

Cavernous sinus meningioma (CSM) with orbital involvement presents a unique challenge to modern-day neurosurgeons. In the modern era of preventive medicine with enhanced screening tools, physicians encounter CSM more frequently. An indolent natural history, late clinical presentation, close proximity to vital neurovascular structures, poor tumor-to-normal tissue interface, and high risk of iatrogenic morbidity and mortality with aggressive resection add to the complexity of decision-making and optimal management of these lesions. The clinical dilemma of deciding whether to observe or intervene first for asymptomatic lesions remains an enigma in current practice. The concepts of management for CSM with orbital involvement have gradually evolved from radical resection to a more conservative surgical approach with maximal safe resection, with the specific goals of preserving function and reducing proptosis. This change in surgical attitude has enabled better long-term functional outcomes with conservative approaches as compared with functionally disabled outcomes resulting from the pursuit of anatomical cure from disease with radical resection. The advent of stereotactic radiosurgery as an adjunct tool to treat residual CSM has greatly shaped our resection principles and planning. Interdisciplinary collaboration for multimodality management is key to successful management of these difficult to treat lesions and tailor management as per individual's requirement.

Keywords
- cavernous sinus meningioma
- multimodality management
- stereotactic radiosurgery
- treatment strategy
- orbital involvement

Introduction

Cavernous sinus meningioma (CSM) is the most common primary cavernous sinus (CS) lesion. Tumors located in the CS represent 1% of all intracranial neoplasms, and 41% of them are CSMs.[1] These lesions are most prevalent in women in their 3rd/4th decade of life.[1,2] CSMs often involve the sphenoorbital region over and beyond the CS proper, which may lead to visual decline and proptosis, due to either direct compression or secondary effects of bony hyperostosis. The CS is described as an anatomical jewel box, hidden beneath the temporal lobe in the middle cranial fossa extending from the superior orbital fissure (SOF) anterosuperiorly to Meckel's cave posteroinferiorly. Our current understanding about the intricate surgical anatomy of CS and the development of novel skull base approaches to the CS stems from the pioneering work of neurosurgical visionaries such as Parkinson, Ramsay, Taptas, Hakuba, Dolenc, Umansky, and Kawase.[3–9] Treatment options for CSM include simple observation, radiation, and surgery or a combination of these,[10,11] depending upon the patient's age, general condition, symptomatology, and tumor dimensions. This topic review discusses the natural history, treatment algorithm, indications, and goals of treatment and surgical approaches for CSM with orbital involvement, with special emphasis to the multimodality management and interdisciplinary collaboration.

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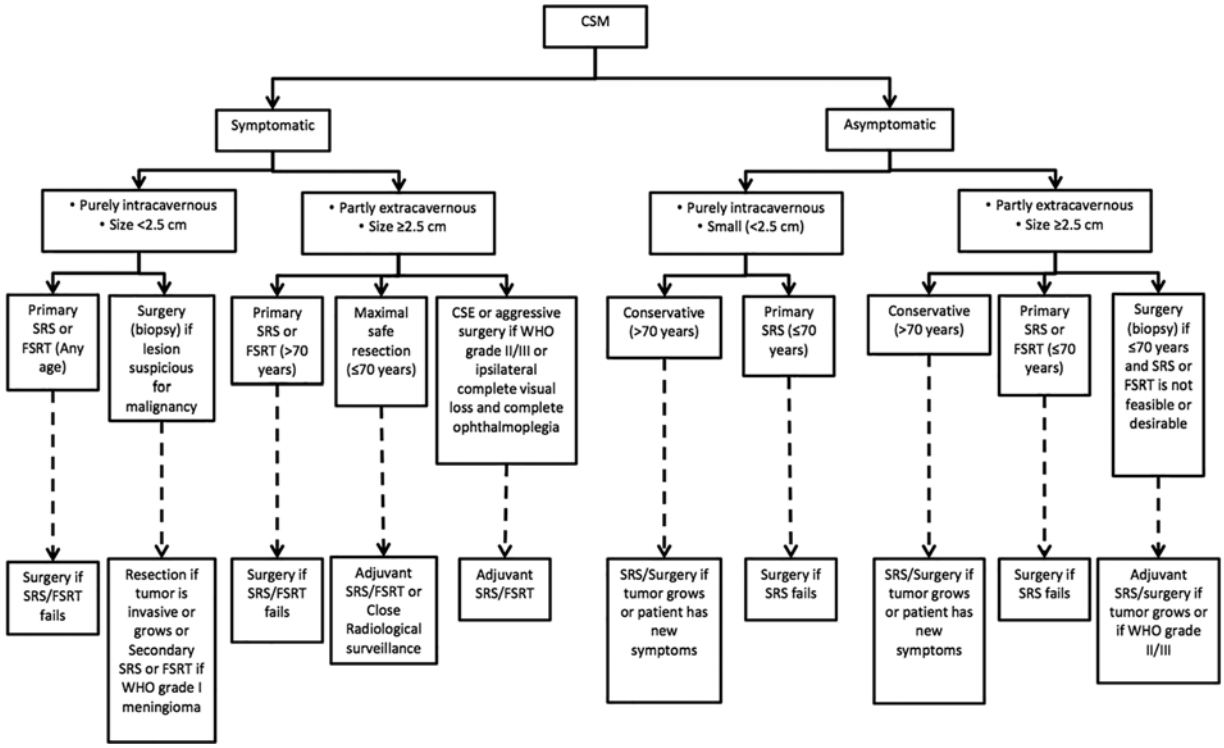

Fig. 1 Practical algorithm for multimodality management of cavernous sinus meningioma. CSE, cavernous sinus exenteration; CSM, cavernous sinus meningioma; FSRT, fractionated stereotactic radiotherapy; SRS, stereotactic radiosurgery.

Pearls and Tips

- A simplified and practical algorithm (►**Fig. 1**) has been provided with this article, which can serve as a roadmap for the management of cavernous sinus meningioma (CSM) tumors and assist in the decision-making process.
- Tumor-associated symptoms, the anatomic localization of the CSM along with its size and extent, the age and functional status of the patient, the tumor pathology, and tumor recurrence all govern the management strategy in CSM patients with orbital involvement.
- Expertise in the field of cerebral revascularization is important in the neurosurgical armamentarium when planning a more radical tumor resection or cavernous sinus exenteration (CSE).
- For purely intracavernous small asymptomatic CSMs in elderly patients, either conservative management with close radiologic surveillance or primary stereotactic radiosurgery or fractionated stereotactic radiotherapy (SRS/FSRT) is a feasible option.
- For small symptomatic CSM, judicious use of primary SRS/FSRT or stereotactic biopsy can help contain tumor growth and ascertain tumor histology, respectively, to facilitate optimal management.
- A primarily extracavernous approach, which leaves the CS proper unopened, is an optimal strategy for most large symptomatic CSM tumors, because it reduces the risk of iatrogenic complications without significantly increasing the risk of tumor progression/recurrence.
- Decompression and dissecting the tumor away from the optic apparatus is vital for institution of adjuvant SRS/FSRT with safety. The approach chosen by the authors is aggressive removal of all tumor compressing the orbit and all involved spheno-orbital bone to enhance function, reduce proptosis, and improve cosmesis.
- Adjuvant RT is a useful option for small intracavernous residual lesions to prevent tumor progression.
- Aggressive attempts at radical tumor resection or CS and orbital exenteration are reserved for patients with ipsilateral complete loss of vision and extraocular movements especially when contralateral function is threatened and in those who have failed previous radiation therapy.
- Multimodality management with interdisciplinary collaboration is key to ensure optimal patient outcome.

Natural History

Although the exact proportion of patients presenting with occult asymptomatic and overt symptomatic CSM lesions is not known, there is a definite trend toward earlier diagnosis of CSM in the natural course of the disease process because of the widespread availability of screening tools and improved

healthcare.[12] Occult asymptomatic CSM lesions are typically benign (World Health Organization [WHO] grade I); atypical and malignant meningiomas comprise only 5% of incidentally diagnosed meningiomas (IDM).[13] Skull base meningiomas tend to have a longer duplication period and lower MIB-1 index than their nonskull base IDM counterparts.[14,15] Nakasu et al[16] classified meningioma growth patterns into three types: no growth, linear growth, or exponential growth. This growth pattern may change with alterations in tumor vascularity, progression of calcification, and acquisition of new mutations.[15,16] Other possible causes for such a dynamic pattern of proliferation status include differential levels of progesterone serum levels, growth-related humoral factors, and growth-related telomere length shortening.[15] Nakamura et al[17] demonstrated a growth rate of 0.19 to 2.62 mL/year (mean 1.24 mL/year) over a mean follow-up of 42.6 months in a series of seven CSM patients. Overall, the factors predicting lower growth rate for IDMs include presence of calcification, hypointensity on T2-weighted magnetic resonance imaging, older age, smaller size (<2 cm), growth rate <10% per annum, and absence of peritumoral edema.[15,17,18] Despite their slow progression, CSMs may present with symptomatic progression due to close proximity to vital neurovascular structures, warranting aggressive management.[14,18] Sughrue et al[18] observed that IDMs in the CS had the highest symptomatic progression rates (61%), followed by those in the cerebellopontine angle (40%), petroclival region (28%), and sphenoid wing (5%). Close radiological surveillance is advised if conservative management is planned for presumed benign CSM lesions, so as not to miss more aggressive radiological differential diagnoses such as hemangiopericytoma, meningeal metastasis, lymphoma, and malignant phenotypes of meningioma.[15] Once symptomatic, CSMs with orbital involvement may present with diplopia, anisocoria, ophthalmoplegia, ptosis, visual field defects, compressive optic neuropathy, proptosis, and facial numbness/pain/dysesthesia.[10] SOF extension often corresponds to more invasive CSM with higher propensity for tumor recurrence.[19–21] WHO grading and MIB index offer true estimates of biological aggressiveness of meningiomas and should govern the decision-making process for use of adjuvant therapy.[10,22]

Indications and Goals of Treatment

The patient's age and general condition and the tumor dimensions, precise anatomical location, and symptomatology govern the treatment algorithm for CSM. We have provided a working algorithm for optimizing the decision-making process in tailoring individualized treatment to CSM patients (►**Fig. 1**). The relative pros and cons of each treatment strategy need to be explained in detail to patients to allow an informed decision based on their expectations and realistic treatment outcomes. Broadly, CSM patients can be divided into those who are asymptomatic and diagnosed incidentally and those who are symptomatic. Asymptomatic patients can be monitored conservatively with radiological surveillance if they are elderly with multiple comorbidities, have a fairly small tumor limited to the CS, and have no evidence of systemic disease with secondary CS involvement.[10,11,22] The key element of treatment in these patients is close follow-up to assess the tumor growth rate and early recognition of new-onset symptoms attributable to tumor, which may necessitate active intervention. These lesions may require stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) to contain tumor growth, symptomatology, and tumor progression.[10,11,22–25]

Aggressive/radical resection is usually not indicated in these patients given the relatively short life expectancy. However, minimally invasive transcavernous biopsy may be required in patients in whom there is a suspicion of an alternative pathology or high-grade meningiomas to optimize the adjuvant therapy. On the other hand, symptomatic healthy, younger patients harboring larger CSM extending beyond the CS proper may require either or surgical biopsy/partial decompression to optimize the tumor control and symptom progression, besides ascertaining the tumor histology and grade.[10,11,22] Upfront SRS/FSRT may be reserved for select patients, although there is associated risk of more aggressive tumor behavior subsequent to RT in some patients. A more radical surgical approach may be required in a select group who demonstrates rapid tumor progression despite first line of management.

In general, the goal of treatment in symptomatic CSM patients with orbital involvement is symptomatic relief rather than anatomical cure. Surgical decompression of any extracavernous tumor portion is indicated in a majority of cases to alleviate the symptoms arising from cranial nerve compression or mechanical proptosis (see below). This results in superior oculomotor function than primary radiation in a long-term study of 50 patients.[26] However, in symptomatic patients harboring small, intracavernous CSMs, surgery with adjuvant SRS/FSRT or primary SRS/FSRT may be offered irrespective of the age group.[23–25] Alternatively, a minimally invasive transcavernous biopsy (via lateral orbitotomy) can be performed if there is any suspicion of malignancy or high-grade meningiomas, which can be then subjected to appropriate adjuvant therapy or a more radical resection (►**Fig. 2**). In contrast, in symptomatic patients harboring large CSM with orbital involvement, upfront SRS/FSRT is restricted to elderly patients with multiple comorbidities where life expectancy is limited. The majority of this subset of patients will require maximal safe resection with or without adjuvant SRS/FSRT for optimal tumor control and symptomatic relief. Radical surgical approach with cavernous sinus exenteration (CSE) is limited to patients with recurrent low-grade (WHO I) CSM, especially in patients where ipsilateral complete visual loss and complete ophthalmoplegia have already ensued (►**Fig. 3**, ►**Video 1**). In each patient, the treatment needs to be tailored as per the individual's needs, with functional preservation taking precedence over anatomical cure from disease.

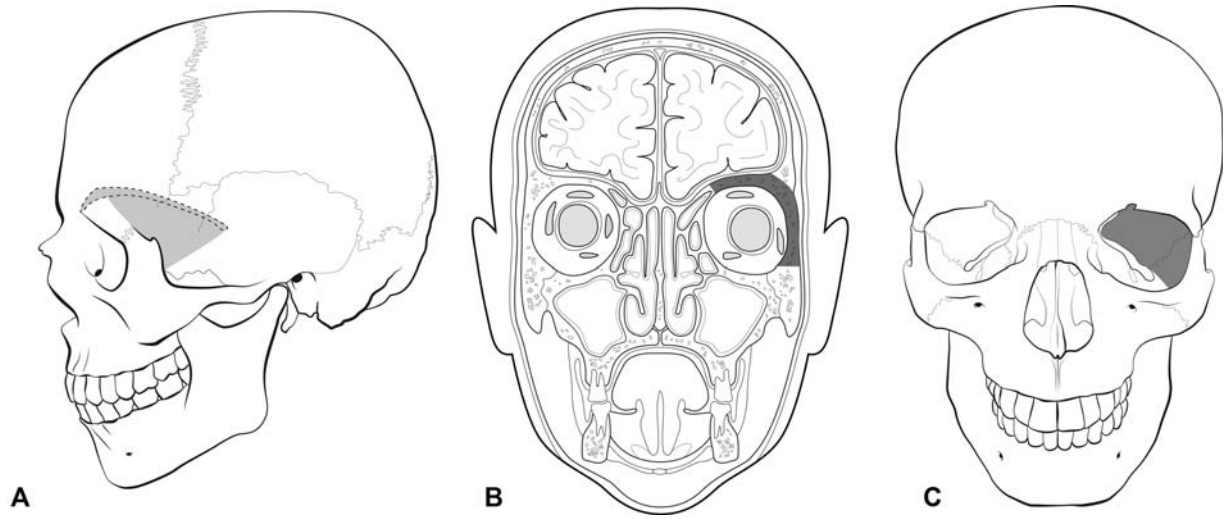

Fig. 2 Lateral orbitotomy. Shading indicates the area of bone removal from an external lateral view (**A**), internal coronal view (**B**), and external coronal view (**C**) during minimally invasive lateral orbitotomy transcavernous approach. Shaded areas include the lateral orbital wall, superior orbital wall, optic canal, and clinoid process. The orbital rim is preferentially preserved. © Department of Neurosurgery, University of Utah.

Video 1

Operative video demonstrating cavernous sinus and orbital exenteration of a recurrent WHO grade I meningioma in a young woman with recurrent disease in the orbit, face, and cavernous sinus. (Used with permission from Altay T et al.)[27] Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0040-1715471.

Surgical Approaches

Surgical intervention for CS lesions can be categorized based on radicality of surgery as transcavernous biopsy, maximal safe resection, aggressive resection, and CSE.

Transcavernous Biopsy

In instances where there is a suspicion of malignant phenotype, a minimally invasive stereotactic or fluoroscopic-guided lesion biopsy can be performed to optimize the treatment strategy. Transsphenoidal, transovale, transmaxillary, and lateral orbitotomy routes can be employed for transcavernous biopsy.[27–30] The senior author prefers a lateral orbitotomy approach (►**Video 2**) for lesions lateral to the carotid

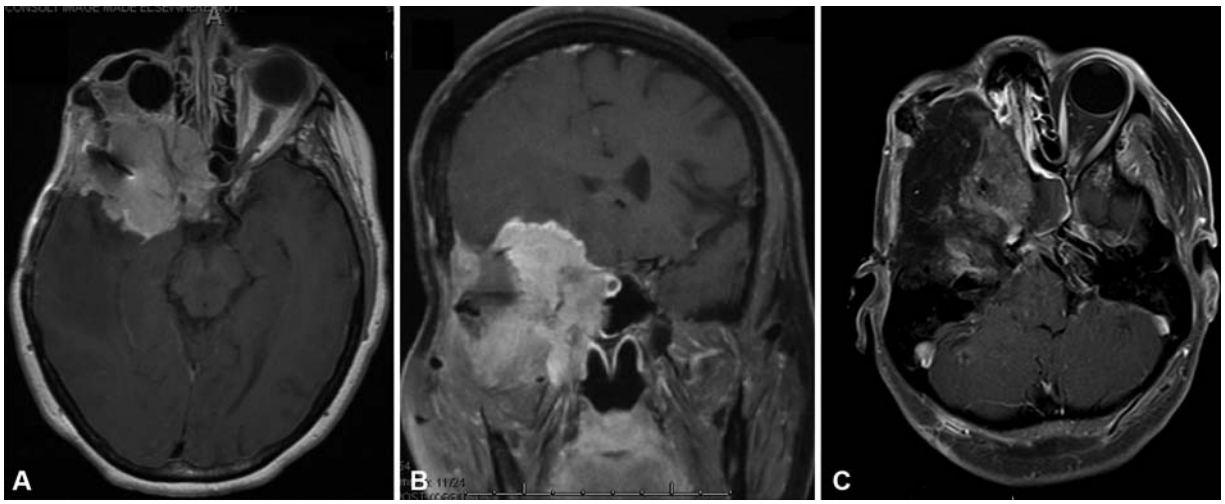

Fig. 3 Extensive recurrent orbital and cavernous sinus meningioma. This 42-year-old woman had a long history of subtotal resection and recurrent orbital and cavernous sinus meningioma. She had undergone ocular resection with placement of prosthesis, with evidence of extensive recurrence within the orbit and right cavernous sinus (**A**, axial and **B**, coronal postcontrast, T1-weighted magnetic resonance imaging [MRI]). Cavernous sinus resection was performed with exenteration of the orbital contents and removal of the right cavernous sinus and cavernous internal carotid artery. Postoperative axial (**C**, postoperative axial postcontrast, T1-weighted MRI) image demonstrates a complete resection, with placement of a thigh free flap.

artery because it offers the opportunity for resection of small CSM tumors through the same operative corridor.[31] Other advantages of this approach include a small skin incision, short incision-to-target distance, minimal soft tissue dissection and blood loss, sparing of temporalis muscle insertion and consequent reduced risk of muscle atrophy, minimal brain retraction, extradural approach with direct trajectory to the anterolateral CS, adequate tissue sampling under direct vision, and reduced hospital stay.[27] For lesions primarily in the medial compartment of the CS (medial to the carotid or inferior-to-anterior loop of the carotid), the endonasal transsphenoidal route is more favorable than the transovale or lateral orbitotomy routes.[29,30]

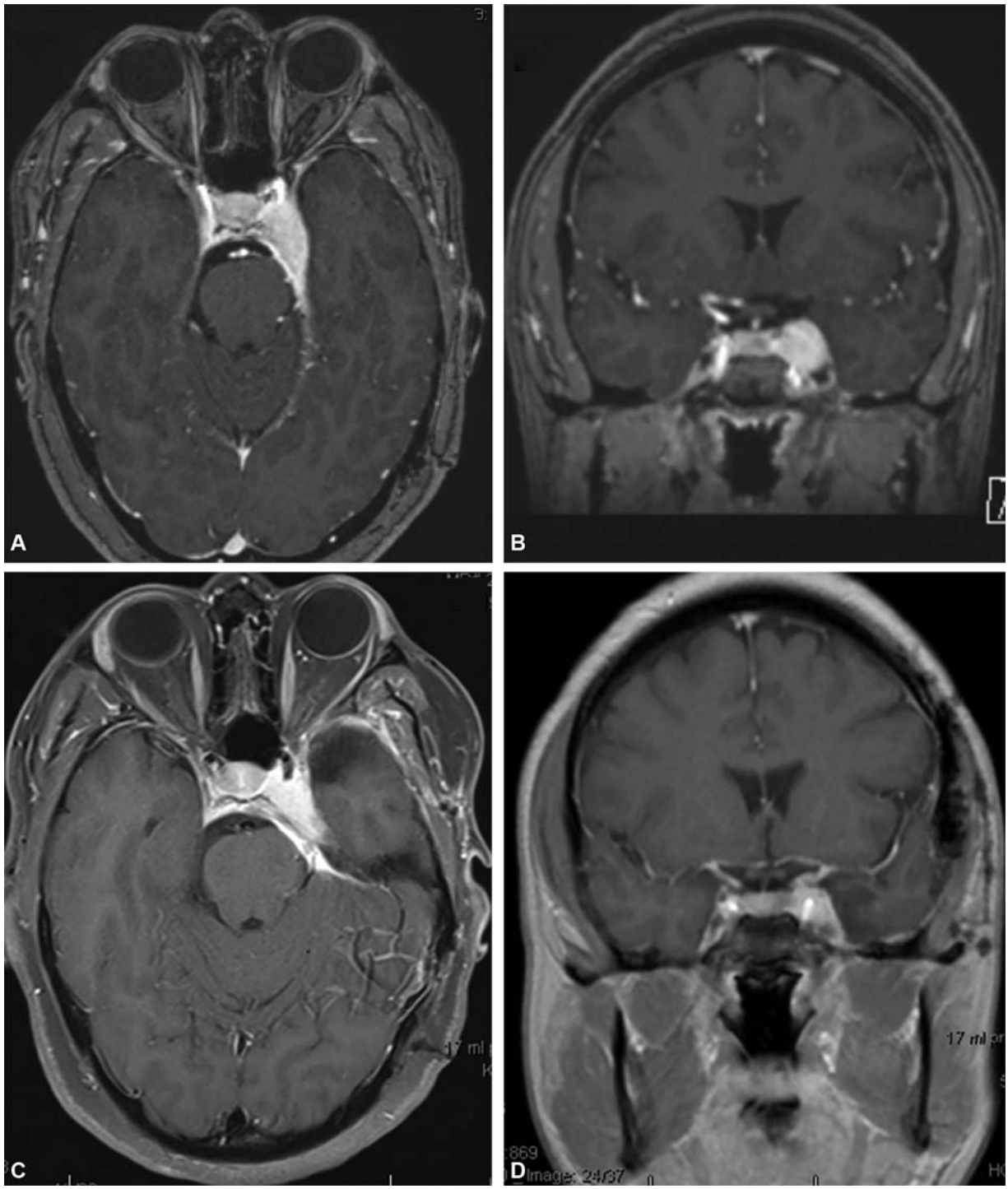

Fig. 4 Postcontrast, T1-weighted magnetic resonance imaging showing a purely cavernous sinus meningioma. This 39-year-old woman presented with progressive left abducens palsy and evidence of an enlarging likely meningioma of the left cavernous sinus (**A**, **B**, preoperative axial and coronal images). She underwent a frontotemporal craniotomy and a left cavernous sinus decompression (**C**, **D**, postoperative axial and coronal images). She experienced improved lateral rectus function and was subsequently treated with stereotactic fractionated radiation therapy.

Video 2

Operative video highlighting the key steps in lateral orbitotomy approach for minimally invasive biopsy of suspected cavernous sinus meningioma. ©Department of Neurosurgery, University of Utah. Online content including video sequences viewable at: https://www. thieme-connect.com/products/ejournals/html/10.1055/s-0040-1715471.

Maximal Safe Tumor Resection of the CSM

This surgical strategy involves partial decompression of the tumor aimed at the resection of the extracavernous part of the tumor and involved dura mater/bone without aggressively chasing the intracavernous tumor remnant to relieve mechanical compression on optic apparatus, orbit, and other vital structures such as the cranial nerves and brain stem to preserve the patient's function (►**Fig. 4**). This approach allows for symptomatic improvement from orbital and neural compression without subjecting patients to the morbidity associated with aggressive intracavernous exploration for residual tumor. Intracavernous tumor exploration does not eliminate the risk of tumor recurrence, even in experienced hands. The residual tumor can then be subjected to secondary SRS/FSRT or close radiological surveillance.[10,11] The senior author practices[26,32] a similar approach for most CSM patients, in whom a standard frontotemporal craniotomy and extradural dissection and decompression of optic nerve, SOF, foramen rotundum, and foramen ovale are performed using a modification of Dolenc's technique of splitting the two layers of the lateral wall of the CS. The initial decompression is followed by piecemeal removal of tumor via narrow operative corridors between the nerves in the lateral wall of CS from the "safe" regions of the CS proper. Any intradural extracavernous component of the tumor is also resected after the involved dura mater is devascularized and removed (►**Video 3**). Any residual tumor left in situ is monitored with serial imaging, and adjuvant radiation therapy (RT) is used only if there is evidence of tumor progression or if the histopathological analysis is suggestive of aggressive tumor biology based on WHO grading and MIB index. Couldwell et al[32] attempted to achieve a minimum of 5-mm interpositional distance between residual tumor and the optic apparatus after surgery to allow safe institution of SRS/FSRT. If required, SRS is typically performed after 3 to 6 months in a single fraction of 12- to 15-Gy marginal dosage. In patients in whom there is a risk of unacceptable radiation spillage to the neighboring vital neurovascular structures, FSRT or intensity modulated radiotherapy with an average dose of 50 to 54 Gy in ~30 fractions are options.[32] Depending on the surgical trajectory needed to access the tumor, transcranial or transfacial approaches can be employed. Transcranial approaches to the CS include Hakuba's/Dolenc's approach (anteromedial approach), a modified Dolenc's approach (anterolateral approach), or Kawase's approach (posterolateral approach).[4,33,34] Similarly, for accessing transfacial routes to the CS, either a transmaxillary or a transsphenoidal approach is used.[29,30,35] A suitable approach to the CS is chosen depending upon the tumor size, location, epicenter and extent, and pathology and the experience/preference of the operating surgeon.

Video 3

Operative video highlighting the key steps in frontotemporal approach for resection of a spheno-orbital meningioma and decompression of the orbit. (Used with permission from Cohen et al.)[31] Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0040-1715471.

Spheno-orbital Meningioma with Associated CS Involvement

Proptosis is typically the presenting sign in patients with spheno-orbital meningiomas (SOMs), although visual deterioration is also frequently observed. Meningioma-associated proptosis (MAP) can be cosmetically and functionally debilitating for patients with SOMs. The senior author has adopted an aggressive surgical approach to the removal of tumor involving the periorbita and orbit in such cases (►**Figs. 5** and **6**; ►**Videos 3** and **4**). In most instances, the orbital rim is not involved with hyperostotic bone and can be left intact; however, all of the involved bone of the orbit is aggressively drilled away, and any intraorbital tumor is removed with the involved periorbita. Care must be taken at the apex of the orbit, in the region of the annulus of Zinn, to avoid damage to uninvolved extraocular muscles. The key to the dissection is to find the tumor–periorbital fat plane at the most anterior extent of the tumor and dissect posteriorly to the region of the orbital apex. If the patient has functional binocular vision, the posterior orbital tumor and cavernous tumor is left in situ after dissection of the lateral wall of the CS (►**Fig. 6** and ►**Video 4**).

Video 4

Operative video illustrating the key steps in frontotemporal approach for resection of spheno-orbital tumor involving lateral cavernous wall and orbit. Tumor within cavernous sinus proper was left in situ. ©Department of Neurosurgery, University of Utah. Online content including video sequences viewable at: https://www. thieme-connect.com/products/ejournals/html/10.1055/s-0040-1715471.

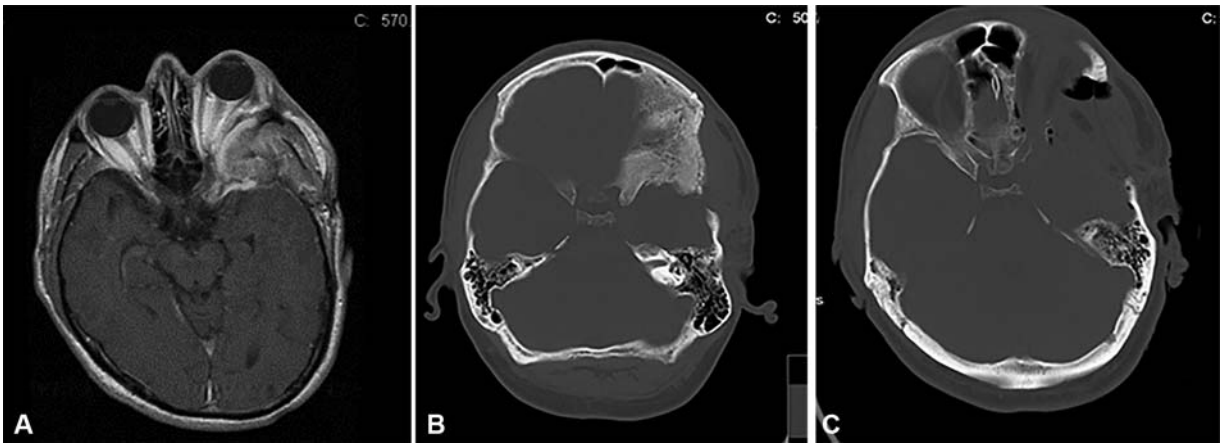

Fig. 5 Extensive spheno-orbital tumor with minimal cavernous sinus involvement. This 45-year-old man presented with orbital congestion, proptosis, and chemosis. Preoperative, postcontrast, T1-weighted axial magnetic resonance imaging (**A**) and computed tomography (CT) (**B**) demonstrate mostly hyperostotic involvement of his left orbit with extensive orbital compression and proptosis. A left frontotemporal craniotomy was performed with gross total resection of the entire bony involvement of his left orbit and decompression of the orbit, evident on postoperative CT (**C**). The left lateral cavernous wall was removed but no soft tissue tumor was evident in the cavernous sinus. He has been followed postoperatively with no additional treatment. His vision remained intact at 3-year follow-up.

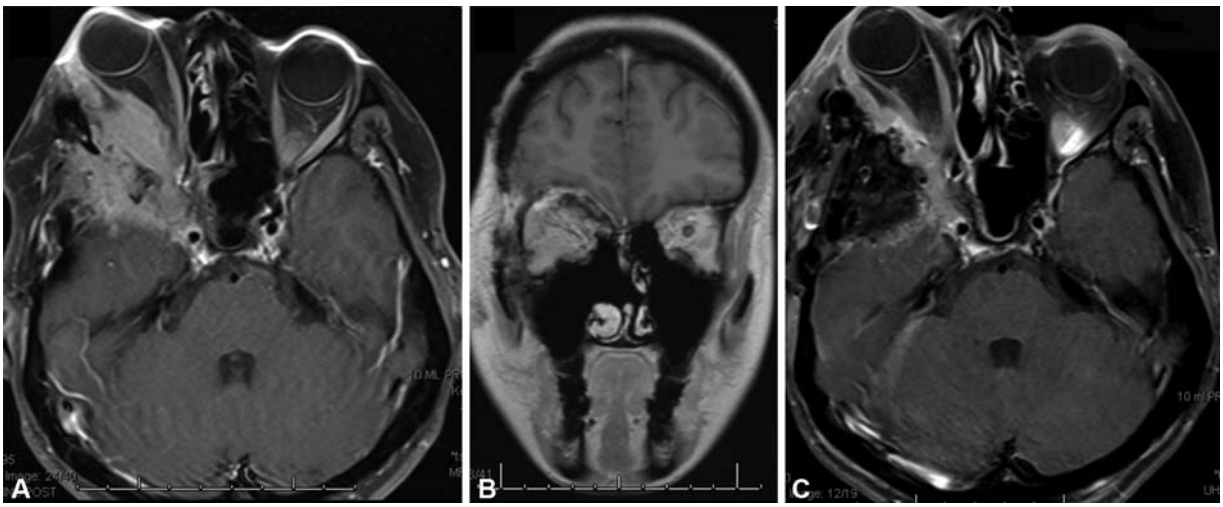

Fig. 6 Preoperative images (**A**, axial and **B**, coronal postcontrast, T1-weighted magnetic resonance imaging [MRI]) of a 47-year-old woman with a recurrent spheno-orbital and cavernous sinus meningioma with progressive visual loss demonstrate orbital involvement with soft tissue, optic nerve compression, and proptosis. The cavernous sinus component was asymptomatic, and the patient had intact oculomotor function. She underwent a right frontotemporal resection of the orbital tumor with decompression of the orbital contents. The lateral wall of the right cavernous sinus was removed, but no intracavernous tumor was resected given she still had intact binocular vision (**C**, postoperative axial postcontrast, T1-weighted MRI). Postoperatively, she had improvement in her vision, and subsequently she underwent radiation therapy of the orbit and cavernous sinus.

In our later experience, the authors have **not** formally reconstructed the orbit following aggressive resection. Enophthalmos was not encountered postoperatively in patients who had presented with proptosis, despite a lack of formal orbital reconstruction. The reason patients with MAP do not experience enophthalmos or significant oscillopsia is not established; however, in our experience, the periorbital tissues show a "woody" or "firm rubbery" consistency, which, we believe, makes the elimination of proptosis difficult but may also account for the lack of significant pulsatile enophthalmos following the extensive decompression. We only reconstruct the orbit on the very rare occasion when the orbital rim must be removed.[36]

Aggressive Surgery

With the evolution of novel skull base approaches, better visualization tools, and refinements in technique of cerebral revascularization, there was a natural progression toward radical resection of CS lesions including CSM in the late 1900s. However, the initial enthusiasm for aggressive CS surgery gradually waned, as the neurosurgical community realized the limits of radical resection in this region. In addition, aggressive surgery was dogged by the ongoing issue of potential tumor recurrences despite aggressive resection and unacceptably high neurovascular morbidity associated with this strategy of resection of tumor within CS proper.[10,11] In addition, the advent of SRS offers excellent

tumor control for residual tumors within margins of the CS proper, with minimal iatrogenic morbidity to cranial nerves and the carotid arteries. This has further bolstered the current philosophy of balancing aggressiveness of surgical resection for these tumors. Factors predicting resectability of CSM include extent of internal carotid artery involvement/encasement, tumor consistency, increased adhesions or loss of anatomic planes from prior RT, and degree of extracavernous extensions involving orbital apex, SOF, and petroclival dura mater. In contemporary microsurgical series, considerable mortality (0–9.5%) and morbidity (17.9–74%) have been reported when resection is extended into the CS proper.[37–42] Thus, there has been a paradigm shift over the past few decades toward a more conservative maximal safe tumor resection approach.

CS Exenteration with or without Orbital Exenteration

The primary indication for CSE, which includes radical resection of CS tumor along with involved neurovascular structures, is recurrent atypical/malignant CSM with orbital involvement despite adequate medical/radiation/surgical treatment and ipsilateral complete loss of vision and extraocular movements or when contralateral function is threatened by progressively growing tumor.[43,44] This oncologic resection is aimed at increasing overall survival and progression-free survival with functional preservation of contralateral neurovascular structures (►**Fig. 3** and ►**Video 1**). Cerebral revascularization with high-flow extracranial–intracranial bypass is often required in this subset of patients depending upon the cross-flow study analysis of both arterial and venous phases.[43,44] Despite adequate planning and execution, CSE carries a high morbidity and mortality rates. George et al[44] performed CSE in 18 patients (including 12 with CSM) including both benign and malignant disease. They observed an 11.1% mortality rate related to the operative procedure, cerebrospinal fluid leak rate of 22.2%, and meningitis in 16.7% patients. Similar results were corroborated in the senior author's experience with reported perioperative mortality rate of 25%.[43] In a larger series, this mortality rate has decreased to less than 10% (unpublished observations).

Multimodality Management and Specialties Involved

A successful outcome for a CSM patient with orbital involvement is governed by close interdisciplinary collaboration among the treating team and physicians involved. Detailed preoperative clinical assessment is performed by a neurosurgical team along with an ophthalmologist to assess the degree of orbital involvement and its impact on visual acuity, visual field, fundus, extraocular muscle movements, proptosis, and sensory deficits along the ophthalmic distribution of trigeminal nerve. Preoperative radiological assessment in consultation with neuroradiologists adds greatly to the planning of an optimal surgical route and anticipated complications due to structures involved. A preoperative angiogram helps ascertain the vascular crossflow across the anterior and posterior communicating arteries via balloon occlusion test and to plan for cerebral revascularization in case of inadvertent internal carotid injury. Selective embolization may also facilitate safe removal of aggressive CSM tumors with acceptable blood loss. Surgical planning and execution involve close collaboration between the neurosurgeon and the ophthalmologist for maximal functional preservation and restoration of any lost function. An otorhinolaryngologist may provide intraoperative assistance for a planned transfacial, transmaxillary or endonasal approach if necessary for tumor removal. Use of intraoperative neurophysiological monitoring for cranial nerve functions and maintenance of adequate depth of anesthesia are other aspects of performing safe surgery for such intricate skull base lesions, with assistance from ancillary branches neuroanesthesia and neurophysiology. Use of motor evoked potentials and somatosensory evoked potentials helps to ascertain long tract physiology intraoperatively, especially helpful in identifying patient position related morbidity. Furthermore, extraocular movement assessment using monitoring for cranial nerves III, IV, and VI helps optimize their functional outcome after surgery. Trigeminal nerve monitoring can also be done primarily for the motor component by monitoring the muscles of mastication. Lastly, use of intraoperative electroencephalography helps assess the depth of anesthesia that can be crucial in case where revascularization is planned with expected long temporary clipping time. Careful neuroanesthesia drug titration is paramount for optimal assessment of intraoperative electrophysiological monitoring. Muscle relaxants are avoided as they can interfere with motor stimulation.

The contribution from a neuropathologist includes precise diagnosis and staging of disease, which is pivotal in tailoring the treatment aggressiveness as per individual patient's tumor biology. Adjuvant therapy in the form of radiation therapy (SRS/FSRT) and chemotherapy/molecular-targeted therapy, which may be required for high-grade tumors, demands close collaboration with the radiation and medical oncologists, respectively. Last but not least, the primary care physician is central to ensure early diagnosis of CSM and timely referral to the specialist for further management.

Conflict of Interest
None declared.

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