A PROSPECTIVE STUDY OF CAVERNOUS SINUS SURGERY FOR MENINGIOMAS AND RESULTANT COMMON OPHTHALMIC COMPLICATIONS (AN AMERICAN OPHTHLAMOLOGICAL SOCIETY THESIS)

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ABSTRACT

Purpose: Cavernous sinus surgery is considered neurosurgically feasible. A systematic review of patients undergoing cavernous sinus procedures for meningioma was undertaken to determine whether cavernous sinus surgery could be performed with an acceptable level of iatrogenic-induced dysfunction.

Methods: Fifty-six patients undergoing 57 cavernous sinus surgical procedures performed by a single senior neurosurgeon were systematically evaluated to determine the consequences of surgery. Quantitative assessment of afferent (acuity, fields, pupil) and efferent function was stressed.

Results: Five of 20 patients (25%) with preoperative optic nerve dysfunction improved, but vision worsened in 6 (30%), including 4 (20%) whose vision deteriorated to no light perception. Four (11%) of 37 patients developed newly acquired optic neuropathy. No patients with preoperative third nerve palsies (19) cleared, although one improved. All 57 patients had evidence of some cranial nerve dysfunction (III, IV, V, or VI) immediately after surgery. Eight patients with long-term follow-up had complete sixth nerve palsies (7 preoperatively), and 4 had complete third nerve dysfunction (none in patients normal preoperatively). Nine (16%) had evidence of aberrant regeneration of the third nerve, and 12 (21%) developed neurotrophic keratitis.

Conclusions: Cavernous sinus surgery results in transient worsening of third, fourth, fifth, and sixth cranial nerve function. Cavernous sinus surgery carries a high risk of worsening ocular motor disorders and producing new ones. Preexisting cranial nerve dysfunction (other than optic nerve) rarely improves. Patients and physicians should be aware of the potential for ophthalmic complications in addition to the more generalized risks of neurosurgery (eg, cerebrospinal fluid leak, infection, stroke).

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INTRODUCTION

Although it is clear from the neurosurgical literature that the mortality associated with cavernous sinus surgery is "acceptable," it has been far less clear whether these procedures have resulted in ophthalmic benefit. Most series refer to improvement without any quantitative assessment. In 1965 Dwight Parkinson[1] directly approached a vascular lesion within the cavernous sinus in a procedure requiring hypothermia and partial circulatory arrest. This was the beginning of the modern era in cavernous sinus surgery, the last area of uncharted territory in neurosurgery. Literally hundreds of articles have been published since then, detailing surgical approaches to various lesions in and around the cavernous sinus. The ability to operate successfully within this area is largely predicated on an improved understanding of the anatomy and pathology in the parasellar region and the development of modern neuroimaging. Cavernous sinus pathology is not infrequently revealed on imaging studies obtained for other unrelated reasons. The majority of patients, however, are still diagnosed because of ophthalmic complaints, including decreased and double vision.

Although the survival rate in cavernous sinus surgery has been generally good, there has been reported morbidity, including damage to the second, third, fourth, fifth, and sixth cranial nerves, all of which have a significant impact on visual function. It is somewhat surprising that little ophthalmic attention has been paid to this recent tendency toward more aggressive cavernous sinus surgery. This study was undertaken to determine the safety of cavernous sinus surgery by prospectively following a series of patients undergoing aggressive cavernous sinus surgery. Evaluations of function were designed to be done as quantitatively as possible in the hope of detecting any improvement or worsening of visual function that could be attributed to the surgery. It was hoped that the data would help both patients and surgeons to devise appropriate treatment strategies.

In essence, this study seeks to record the natural history of cavernous sinus surgery. A single surgeon, one institution, and an ophthalmological follow-up provide a unique database to address the following issues:

1. What is the morbidity and mortality associated with cavernous sinus surgery?
2. What are the ophthalmological sequelae?
3. Are these complications of sufficient magnitude to recommend that cavernous sinus surgery not be done?
4. The data are dependent on the one surgeon and his technique. Might a different surgeon and technique produce better results?
5. What are the alternatives to cavernous sinus surgery?

THE HISTORY OF THE CAVERNOUS SINUS AND ANATOMICAL CONSIDERATIONS

The first use of the term *cavernous sinus* is attributed to Winslow,[2] who in 1732 likened the space on either side of the sphenoid body to the corpora cavernosum of the penis. He wrote that "the internal carotid is bathed in the blood of the sinus together with the IIIrd, IVth, Vth, and VIth pairs of nerves." Recent historical reviews point out that this area had been the subject of dissection much earlier

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than Winslow's studies. Understanding the venous anatomy at the skull base required an accurate description of the arterial circulation. Prior to the 16th century, Galen's erroneous teaching that the carotid artery divided into rete mirabile before entering the dura was generally accepted. Wepfer,[3] in 1658, described the path of the carotid artery, including its course through the skull base within a "deep and conspicuous sinus." Even before Winslow, in 1685, Raymundi Vieussens[4] described how the cranial nerves cling to the outer wall of the cavernous sinus. Thus, by the beginning of the 18th century, the basic outline of the anatomy of the parasellar region could be found in the medical literature.

When Ridley[5] suggested in 1695 that the cavernous carotid lay against the lateral wall of the sinus, he laid the foundation for one of the most contentious debates in central nervous system anatomy. The carotid was not put back in its appropriate place until 1932, when Weizenhoffer[6] recognized the normal separation between the cranial nerves and the carotid artery. As recently as 1966, Bedford[7] (after dissecting 34 cavernous sinus specimens) inaccurately described the carotid as directly applied to the lateral wall. One can speculate about the fixation status of his specimens. More recent studies have concentrated on the various venous spaces, lateral, and anterior to and occasionally around, the carotid artery.[8-15]

The major controversy that persists to this day concerns the microscopic anatomy of the venous channels themselves. By his choice of a name, Winslow had assumed a trabeculated venous space. These trabeculations were present in an illustration published by Duke-Elder[16] and in many earlier anatomy texts. Their presence was thought to be responsible for the frequency of thrombosis within the cavernous sinus. Bedford[7] initially challenged the presence of trabeculations, suggesting that the sinus was largely free of obstruction. In 1949,[17] and later in the 1980s,[18,19] Taptas suggested that the area was not an open venous sinus at all, but rather an irregular network of veins. Bonnet,[20] using microdissection and corrosion casts, supported this plexus theory, which was subsequently championed by Parkinson.[21-23] Krivosic,[24] Rhoton and associates,[25] and Hakuba and coworkers[26] have all suggested that there are probably anatomic features of both; that is, trabeculated venous spaces and various venous channels intermixed within the extradural parasellar space. The lateral wall, in particular, may contain venous channels.[13]

The earliest described pathology of the cavernous sinus relates to its vascular origin. Biumi published a description of a carotid cavernous aneurysm in 1765, and Blane described the results of a postmortem on a woman who had died in 1794 with an intracavernous carotid aneurysm. Adams[27] recognized an aneurysm of the cavernous carotid associated with complete ophthalmoplegia and numbness. In his series of intracerebral aneurysms, Bartholow[28] noted a case of a carotid cavernous aneurysm in 1872.

Although various (usually fatal) attempts at draining the cavernous sinus occurred in the 19th century, Krogius[29] is generally credited with the first surgical approach to a "mesothelioma" (likely a meningioma) invading the cavernous sinus. Frazier[30] related the details of a case of cavernous sinus thrombosis, which had been treated surgically in 1900, concluding that "the cavernous sinus is not within the realm of the surgeon's knife." Langworthy[31] suggested that the treatment of cavernous sinus thrombosis "consists in incising and draining the cavernous sinus directly." Prior unsuccessful attempts are also mentioned. He does not detail whether he personally witnessed a successful procedure.

Prior to Parkinson's report in 1965, there was little enthusiasm for surgery in this area. As late as 1978, Trobe and coworkers[32] reviewed a series of 6 cavernous meningiomas and 9 aneurysms and concluded that "craniotomy is not recommended." In 1979 J. Lawton Smith[33] commented that "neither of the two lesions [meningioma or aneurysm] in the cavernous sinus should be considered surgical candidates." At almost the same time, Vinko Dolenc,[34] after careful anatomical studies, undertook a direct surgical attack on intracarotid vascular lesions in 7 patients, without resorting to modification of the circulation. These cases, predicated on Parkinson's pioneering work, were the opening salvo in what has become a barrage of surgical cases involving the cavernous sinus.

ANATOMY OF THE CAVERNOUS SINUS

Embryologically, the cavernous sinus begins as an extradural out-pouching between the temporal lobe dura and the perichondrium of the basichondrocranium.[35,36] Venous channels develop within this area to form the cavernous sinus in the basal epidural space. The lateral wall contains the third, fourth, and first division of the fifth cranial nerve along with their own dural sheaths.[37,38] These sheaths variably merge to form a more or less continuous inner lining that is subsequently overlaid by the medial dura of the temporal lobe. The sheaths themselves represent a relative weak spot in the dura surrounding the cavernous sinus and often serve as a conduit for secondary cavernous sinus involvement from surrounding meningiomas.[39] In planning for surgery in this area, it is best to remember its embryological origin.[40,41]

Anatomically,[42] the cavernous sinus can be seen as an extradural parasellar extension of the contents of the orbit.[43] The medial wall of the cavernous sinus directly continues as the medial periorbita, through the superior orbital fissure. The lateral wall of the cavernous sinus is formed by the condensation of the sheaths of the third, fourth, and first division of the fifth cranial nerves. This sheath condensation extends anteriorly to join the orbit at the superior orbital fissure, where the lateral wall fuses with the lateral periorbita. Kehrli and colleagues[9-11] have emphasized the true extradural nature of the cavernous sinus in a series of articles.

The bones adjacent to the cavernous sinus include the body of the sella (medially) and the floor of the middle cranial fossa (inferiorly). The floor of the cavernous sinus extends between the foramen rotundum (anteriorly) and the foramen ovale (posteriorly and laterally). The carotid artery enters the posterior aspect of the cavernous sinus through the floor overlying the foramen lacerum. The anterior clinoid, which represents the terminal portion of the lesser wing of the sphenoid, forms the anterior aspect of the lateral wall of the optic canal. Its underlying strut separates the superior orbital fissure from the optic canal. This potential space can be made into a working space by the neurosurgeon. Removal of the anterior clinoid reveals the anterosuperior aspect of the cavernous sinus, and access is provided via the roof of the cavernous sinus through the (anteromedial) triangle formed by the optic nerve (medially) and

the third nerve (laterally).[44] Surgical approach through this space is a particularly convenient route to the anterior intracavernous carotid artery (see below).

The dural roof of the cavernous sinus continues[14] as the diaphragma sellae, which covers the sella turcica enclosing the pituitary gland. The roof of the cavernous sinus extends posteriorly to the clival dura and laterally to the posterior clinoids. The posterior clinoids also mark the rostral termination of the dorsum sellae. The base of the posterior wall of the cavernous sinus is marked by the petroclinoid (Gruber's) ligament, which connects the posterior clinoid to the petrous apex.[45] This dural attachment forms the roof of Dorello's canal, which contains the sixth nerve after it enters the dura, and the inferior petrosal sinus on its way to the jugular bulb.

The carotid artery, the largest structure contained within the cavernous sinus, enters the sinus from the carotid canal, which is located within the petrous bone, where the carotid runs just under the greater superficial petrosal nerve and above the Eustachian tube. At the medial end of the carotid canal, it makes a turn (Dolenc's lateral loop)[44] to rise over the area of the foramen lacerum. It enters the floor of the cavernous sinus just medial to Meckel's cave and makes another loop (Dolenc's medial loop) to travel forward in its intracavernous horizontal section. As mentioned, the carotid is usually in close contact with the lateral sella wall and thus the medial wall of the cavernous sinus. A condensation of fibrous tissue separates it from the sella. At the anterior end of the horizontal section, the carotid artery makes its final loop (anterior), reversing its course just under the anterior clinoid and medial to the optic nerve. Two condensations of fibrous tissue, the proximal and distal loops, surround the carotid below and above the clinoid and mark the passage of the carotid, first out of the cavernous sinus, and then into the intradural space.[46-48] Thus the clinoidal portion of the carotid artery is still extradural.

The lateral wall of the cavernous sinus[37] contains the third nerve superiorly, the fourth nerve just below it, and the first division (the ophthalmic) of the fifth nerve. The second division of the fifth nerve (maxillary) forms the inferior lateral border of the cavernous sinus and parallels the first division. The maxillary division runs through the foramen rotundum located just below the inferior aspect of the superior orbital fissure, which transmits the ophthalmic division. As the cranial nerves approach the superior orbital fissure, the third nerve divides into a superior and inferior division. The fourth nerve travels superiorly to cross laterally to medially above the branches of the third nerve. The ophthalmic division of the fifth nerve divides into 3 branches: the lacrimal, frontal, and nasociliary. The blood supply to the cranial nerves within the cavernous sinus has been studied in detail.[49-56]

Textbooks older than 50 years often list the ophthalmic artery as the first major branch of the intracranial internal carotid artery. Actually, 2 variable sets of carotid branches exit in and around the cavernous sinus.[57,58] They are particularly important because they supply blood to the surrounding dura and to the cranial nerves running in and around the cavernous sinus. The first of these branches, the meningohypophyseal trunk,[56] divides into the tentorial artery, the dorsal meningeal artery, and the inferior hypophyseal artery. The tentorial artery supplies the cranial nerves as they enter the cavernous sinus posteriorly. The second major vessel is the inferolateral trunk,[51,52,55] which subsequently divides into 4 branches. The superior 2 branches are critical to the blood supply to the intracavernous third and fourth cranial nerves. Significant collateralization in this area usually protects these nerves, even if the inferolateral trunk is disturbed. Terminal dural branches from the middle meningeal artery (entering the skull through the foramen spinosum) connect with the branches of the inferolateral trunk to form the artery of the foramen rotundum (accompanying the second division of cranial nerve V) and the artery of the foramen ovale (accompanying the third division of the trigeminal nerve). The inferolateral trunk is variable in location, but is found in the majority of specimens studied. It may rarely arise as a branch of the meningohypophyseal artery at the posterior aspect of the cavernous sinus. There are additional collaterals that join the inferolateral trunk to the accessory meningeal branches that supply the pterygoids and the inferotemporal area below the middle cranial fossa.

Besides the venous channel, the cavernous sinus also contains the sixth nerve, which is located just lateral to the carotid artery, and the sympathetic plexus, which enters the cavernous sinus within the carotid sheath.[59-64] The pericarotid sympathetic plexus coalesces to form a variable number of trunks, which exit with the sixth nerve to join branches of the fifth nerve entering the superior orbital fissure. In addition, due to its embryological and anatomical connection to the orbit, it is not surprising that fat can be found[10,65] microscopically in 10% or more cases. This finding has produced some confusion because the low signal intensity within the cavernous sinus on computed tomography has suggested a pathological process in patients with other surrounding pathology.

The venous connections into and out of the cavernous sinus include the superior ophthalmic vein anteriorly and various cortical branches that may enter the cavernous sinus directly. In addition, in a minority of cases, the inferior orbital vein may directly enter the cavernous sinus, instead of indirectly via its connection to the superior ophthalmic vein anterior to the superior orbital fissure. Outflow from the cavernous sinus usually proceeds via the inferior petrosal sinus, which exits the posterior aspect of the cavernous sinus and runs directly down to the jugular bulb or through the superior petrosal sinus to the lateral sinus. In addition, there are variable connections to the pterygoid inferiorly through a plexus of veins and to the opposite cavernous sinus through an intrasellar connection both anterior and posterior to the pituitary fossa.[66] Finally, there may be a variable venous plexus that extends down the clivus posteriorly and under the dural aspect of the middle cranial fossa inferiorly and laterally.

Because there are no valves within the cavernous sinus, blood flow can easily be reversed, particularly in the setting of arterial injection into the cavernous sinus either directly from the carotid artery or indirectly through internal or external dural branches. In the setting of a carotid cavernous fistula, flow often reverses into the superior ophthalmic vein, thereby producing evidence of orbital congestion as well as secondary increased intraocular pressure (related to the problems with ocular venous outflow). This flow reversal results in the myriad ophthalmic manifestations of a carotid cavernous fistula.[67-71]

Although the cavernous sinus is separated from the afferent visual pathway by the optic strut anteriorly and by the increasing subarachnoid separation between the optic nerve and the roof of the cavernous sinus posteriorly, pathology arising in the cavernous sinus can extend superiorly to affect the optic nerve or chiasm. Often extracavernous extension elevates the optic nerve, compressing

it against the falciform fold in the dura at the posterosuperior exit of the optic canal.[72] This results in arcuate (usually inferior) visual field defects and variable acuity loss.

PATHOLOGY OF THE CAVERNOUS SINUS

As mentioned, pathological involvement of the cavernous sinus was only rarely identified prior to the advent of imaging technologies. Vascular pathology was an exception, however. The florid ophthalmic manifestations of a carotid cavernous fistula were described in the 19th century. Reverse venous flow within the orbit produces variable ocular motor palsies, pain, and sensory loss as a result of arterialized blood dumped directly into the cavernous sinus.[28,69,71] Venous engorgement may produce chemosis, proptosis, and a characteristic increased pulse pressure. Low-flow fistulae were more difficult to detect and, prior to the introduction of angiography, probably were ignored.

A second exception was cavernous sinus thrombosis. In 1854, MacKenzie,[73] in his 4th edition, reported on a case of a Welsh laborer who was struck in the orbit with a clay pipe and who eventually succumbed to a cavernous sinus infection. At autopsy a retained foreign body was found within the cavernous sinus. Much of the early ophthalmic literature that dealt with the cavernous sinus reported cases of septic cavernous sinus thrombosis. This was usually secondary to head and neck infectious sources commonly originating in the sinuses, teeth (dental caries), and the ears (mastoiditis and petrositis).[74] The prognosis in pre-antibiotic days was dismal, since death almost always occurred within days; Frazier[30] estimated that only 7% survived.

Medical science was slow to recognize that mass lesions in the parasellar region could produce cranial nerve palsies. In the 19th century, most cranial nerve palsies were attributed to inflammatory, toxic, or metabolic pathology that was thought to be intra-axial. Infectious processes, including syphilis and tuberculosis, were frequently blamed for the development of ophthalmoplegia. Gowers[75] recognized that most intra-axial pathology usually affected the ocular motor nerves bilaterally. He did, however, note that "paralysis of the ocular muscles may be due to disease of the nerves in the orbit or at the base of the brain." Swanzy,[74] writing in Norris and Oliver, noted that "tumors and inflammatory products about the cavernous sinus are very liable to cause partial or complete third-nerve paralysis, along with partial or complete paralysis of some or all of the other orbital nerves, as well as of the optic and olfactory nerves." Langworthy[31] (in Casey Wood's *The American Encyclopedia of Ophthalmology*) noted that "from time to time observers report neoplasms involving the cavernous sinus in which the eye symptoms vary according to the extent and character of the growths." Nettleship, quoted by Swanzy,[74] reported a "sarcoma" that occupied the right cavernous sinus resulting in total ophthalmoplegia. He recognized that despite mild proptosis, the absence of optic nerve dysfunction suggested sparing of the orbital apex.

Wilbrand and Saenger[76] summarized previously reported cases of skull base pathology resulting in ocular motor problems in a text published at the turn of the century. Frank Walsh[77] discussed cavernous sinus thrombosis and carotid cavernous fistulae, but in the first edition of his text on clinical neuro-ophthalmology had little to say about cavernous sinus neoplasms. Although Duke-Elder[16] showed a picture of a patient with ptosis and probable ophthalmoplegia (captioned as a "para-orbital tumor"), he failed to discuss the possibility of neoplastic lesions of the cavernous sinus.

Neoplastic pathology was often overlooked as a cause of neurogenic ophthalmoplegia. Duke-Elder[78] listed tumors as only one of 6 possible etiologies (including acute and subacute inflammatory diseases, metabolic diseases, intoxications from exogenous poisons, vascular lesions, and trauma). In his list of the causes of chronic and progressive ophthalmoplegia (in which he included syphilis, multiple sclerosis, diffuse sclerosis, syringomyelia, and amyotrophic lateral sclerosis), he omitted mass lesions entirely. In localizing intracranial tumors, he mentions the brainstem, pons, medulla, supratentorial regions (causing herniation), and the meninges, but without discussing the parasellar region.

In view of the fact that meningiomas make up the majority of cavernous sinus lesions, it is remarkable that Cushing and Eisenhardt[79] did not identify the cavernous sinus as a significant primary location for meningiomas. Only 5 tumors were identified as primarily parasellar in the 294 patients they studied. They did recognize that tumors originating in Meckel's cave, the medial sphenoid wing (including the anterior clinoid), and the floor of the middle cranial fossa could secondarily involve the tissues of the cavernous sinus. Undoubtedly, extension into the cavernous sinus was responsible for some of the impairment of the second through sixth cranial nerves noted in many of their patients.

Individual case reports appeared during the first 2 decades of the 20th century,[80] but it was Foix[81] who first reported on a series of cases with cavernous sinus pathology. This pioneering work was followed by a 1938 report from Geoffery Jefferson[82] on 55 saccular aneurysms of the cavernous sinus. Jefferson also recognized the importance of these findings to ophthalmologists, and when he delivered the 1952 Bowman lecture,[83] he described the features of 112 cavernous sinus lesions (including 22 traumatic cases with 17 carotid cavernous fistulae, 38 aneurysms, and 52 tumors). He reported that there was "little in the structure of the cavernous sinus to furnish material for primary neoplasms." Thus, the majority of tumors in his series were related to extrinsic invasion, most commonly from the nasopharynx or paranasal sinuses.

Current data would suggest that he was correct about truly primary tumors of the cavernous sinus. Only aneurysms are literally primary within the cavernous sinus.[84,85] Although meningiomas can arise from the dura of the lateral wall of the sinus, most originate from dura covering the sphenoid or petrous bones and secondarily invade the cavernous sinus. These tumors have a propensity for following the sheaths of the cranial nerves as they enter the lateral wall of the sinus.[39] Jefferson listed 3 meningiomas (out of 346 meningiomas that he had treated) that were located primarily within the cavernous sinus. He also included 4 "neurinomas" involving Meckel's cave and one case of neurofibromatosis. The majority of his cavernous sinus cases was malignant and included 23 nasopharyngeal carcinomas, 8 carcinomatous metastases, 2 adamantinomas, and 1 chordoma.

Of 102 patients from the Mayo Clinic reported on in 1970,[86] tumors occurred in 70 (69%), aneurysms or fistulas in 19 (19%), and

inflammation in 9 (9%). Forty-three (61.4%) of the 70 patients with neoplastic disease suffered from metastasis. This included distant spread in 23 patients and local spread (nasopharyngeal carcinoma in all but one) in 20. Only 14 patients (20% of those neoplastic lesions) had primary intracranial lesions including 6 pituitary adenomas, 3 meningiomas, 2 craniopharyngiomas, 2 sarcomas, and 1 neurofibroma.

More recently (in 1996), James Keane[87] published an epidemiological study reviewing 151 patients who presented with the "cavernous sinus syndrome" during a 26-year period. Inclusion criteria for the study included evidence of multiple cranial nerve palsies. This was also a very select series, because these individuals were evaluated while they were patients at the Los Angeles County Hospital. It is thus not surprising that trauma occurred in 36 patients (24%). An additional 17 patients (11%) had conditions secondary to surgical trauma following neurosurgical procedures. This high frequency of trauma diluted the percentage of tumors (45 [30%]) and aneurysms (9 [6%]). Nineteen patients (13%) had evidence to suggest inflammation and an additional 15 patients (10%) were thought to have "likely" inflammation. The other interesting feature in this series is that although the incidence of nasopharyngeal carcinoma had declined (from 46% in the Jefferson series to 22% in the Keane series), it still was the single most frequently occurring tumor. In addition, metastatic disease occurred in 8 patients and lymphoma in an additional eight patients (18% each). Invasive pituitary adenomas were recognized in 8 patients (18%) and meningiomas in only 4 patients (9%).

The major difference between the previous studies and this most current publication has been the advent of neuroimaging. Introduced in the United States in 1975, computed tomography[88-90] and, more recently, magnetic resonance imaging[91-96] have completely revolutionized our ability to detect lesions in the cavernous sinus.[97] Prior to that, cavernous sinus pathology was detected almost solely on the basis of clinical findings, most commonly diplopia (due to involvement of the third, fourth, and sixth cranial nerves). Less commonly, patients were evaluated for numbness or pain. Prior to 1975 it was rare for cavernous sinus pathology to be recognized without evidence of progressive cranial nerve dysfunction.

Recent larger surgical series provide additional epidemiological data (see Appendix B). In a series of 63 cases treated by Dolenc and colleagues[98] between 1980 and 1985, there were 40 cases of meningiomas, 2 cases of malignant meningiomas, 7 pituitary tumors, 4 neurilemomas, and 3 plexiform neurofibromas. Other pathology included fibrous dysplasia, epidermoid, cholesteatoma, myxoma, and fibrosarcoma. In 154 cases collected from 3 institutions, Al-Mefty and coworkers[99] reported 42 meningiomas, 35 pituitary tumors, 32 aneurysms (including 19 ophthalmic and 13 carotid), and 4 fistulae. He also listed 15 nasopharyngeal carcinomas and 12 other malignant tumors, including 4 metastases, 4 paranasal sinus carcinomas, 2 adenoid cystic carcinomas, and 2 myxochondroid sarcomas. This increased representation of meningiomas (and benign tumors in general) may have a component of referral bias.

The proliferation of reported cavernous sinus pathology is indicative of the substantial improvement in our diagnostic techniques, especially neuroimaging, rather than an actual increase in the frequency of these lesions. This interpretation is supported by the decreasing incidence of diplopia and decreased vision as primary symptoms in referred patients and increasing frequency of pain and headache. In many of these patients, the presence of cavernous sinus pathology was uncovered fortuitously, when imaging studies were ordered for nonspecific headache syndromes or migraine. Without numbness, pain has a low probability of indicating a cavernous sinus lesion.

In a retrospective epidemiological study (Appendix A), files of patients seen in the neuro-ophthalmology unit at the University of Virginia were screened for cavernous sinus involvement. A total of 347 patients (230 women and 117 men) seen during the last 12 years were selected as having been coded for cavernous sinus pathology. Neoplasia affected the largest group, that is, 236 (63%) of 374 cases. Of the tumorous growths, meningiomas (118) made up one-half with a smaller contribution of 35 pituitary tumors of 12 neurilemomas, and 6 cavernous hemangiomas. Pituitary tumors are rarely reported within the cavernous sinus.[100,101] Carcinomas were much less common (only 25 cases) and were scattered among the various types. The other major diagnostic group consisted of vascular lesions (97 cases), including 45 aneurysms and 52 fistulae, both direct and indirect. Inflammatory lesions were generally uncommon; 4 cases of cavernous sinus thrombosis, 7 presumed Tolosa-Hunt syndrome (one with biopsy confirmation), 2 Zoster inflammation, 2 granulomatous disease (one case related to sarcoid), 3 aspergillomas, and 2 mucormycosis. Patient ages ranged from 5 to 84 years, with a mean of 51 years at presentation. In analyzing the larger diagnostic groups separately, only neurilemomas occurred in patients at a significantly younger age (31 years) than the overall population.

Meningiomas are the most frequently occurring tumor in all modern lists. Although rare cases of entirely intracavernous meningiomas occur, the majority (as suggested by Cushing) arise from the surrounding dura (Figure 1). They may originate from the anterior clinoid.[99,102] Delfini and colleagues[103] reported on 16 patients with meningiomas arising from Meckel's cave. These patients had usually presented with symptoms of trigeminal dysfunction. Clival meningiomas can also invade the cavernous sinus, in which case they commonly produce sixth cranial nerve dysfunction given that Dorello's canal is affected.[39,104] Although clival meningiomas most frequently cause brainstem dysfunction (due to posterior extension), many expand anteriorly, affecting the posterior cavernous sinus. This involvement increases the morbidity associated with surgical approaches.[105] Petroclival meningiomas may also be very extensive and difficult to excise completely.

MATERIALS AND METHODS

NEURO-OPHTHALMIC EVALUATION

After obtaining institutional review board (IRB) approval, a series of patients with cavernous sinus pathology evaluated between November 1988 and June 1995 were analyzed preoperatively and postoperatively for changes in their neuro-ophthalmic status. These patients were drawn from a series of 347 patients coded as having cavernous sinus surgery at the University of Virginia Health System

over a specified period. The study interval is restricted to 1988-1995 because cavernous sinus surgeries were no longer routinely performed post-1995. Patients were the subject to a neuro-ophthalmic assessment before and immediately following surgery. These studies were repeated with as much long-term follow-up as possible. In planning the study, tests were selected to be quantitative.[106] These included measuring parameters of afferent and efferent function. All patients were evaluated with best-corrected Snellen visual acuity, near visual acuity, and automated static perimetry (when feasible). Asymmetric optic nerve function was quantitated through the use of neutral density filters (.3 log steps) to measure afferent pupillary defects. Facial sensation was assessed grossly, and corneal sensation was quantitated with an esthesiometer. Ocular motility was evaluated by gross ductions, and eye movements were recorded using 9-cardinal position photography. Versions were assessed with dissociative testing by using a Maddox rod and, when possible, quantitated further with the aid of a Hess screen performed at a 1 meter test distance.[107,108] Subsequent follow-up evaluations also included the use of binocular single-vision field testing by using a Goldmann perimeter in those patients with areas of fusion and diplopia. When there was evidence of optic nerve involvement, additional quantitation was obtained with photographic records of the optic nerve head and posterior pole.

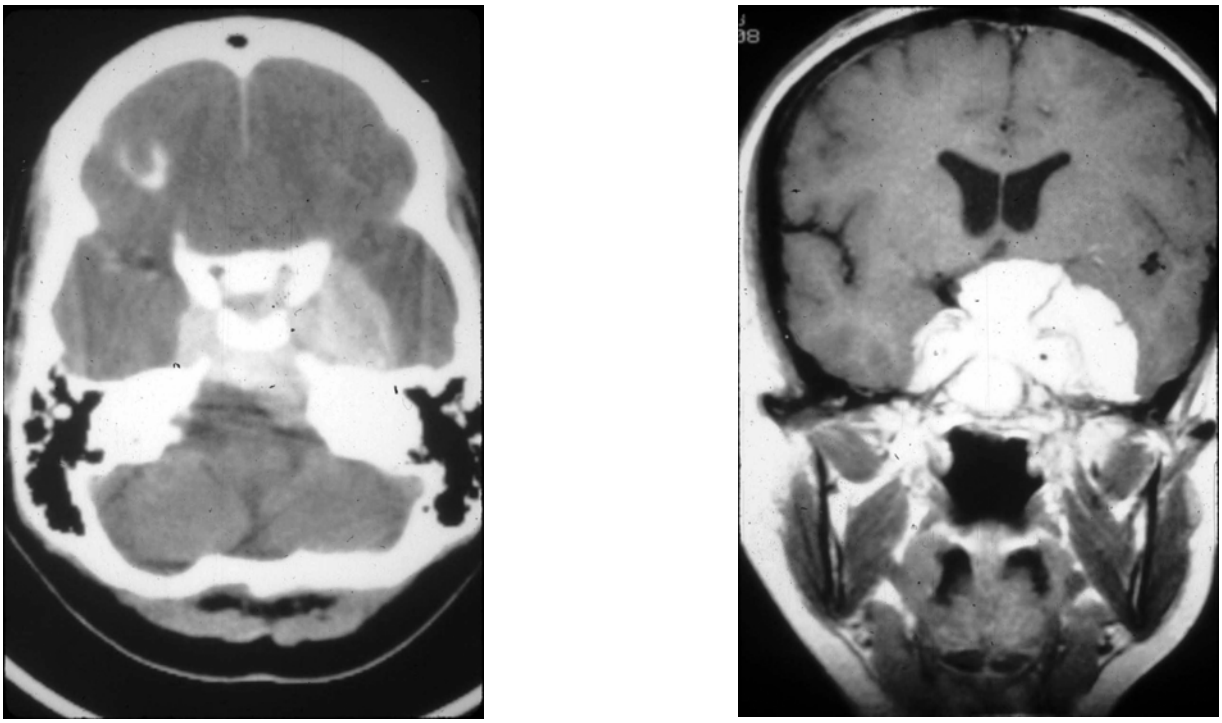

FIGURE 1

Case 2. Computed tomography (left) and magnetic resonance imaging (right) scans of a patient with a long history of a known skull base meningioma. The tumor can be seen to be encasing the carotid and middle cerebral arteries.

The initial series consisted of a total of 81 patients who underwent 82 cavernous sinus surgical procedures. Of these patients undergoing cavernous sinus surgery, 56 were found postoperatively to have meningiomas (Table 1). This series included 16 men and 40 women whose ages ranged from 23 to 81 years with a mean of 51 years. One man had a recurrence and underwent a second procedure to extirpate the cavernous sinus meningioma. The time from initial development of symptoms to diagnosis ranged from less than 1 week to 168 months, with a mean of 18.9 months. Diagnosis was delayed by more than 2 months in 23 of 57 cases (as much as 13 years). In one remarkable case the diagnosis was delayed for 2 years in spite of the fact that the patient had previously had a meningioma resected 10 years earlier. Diagnoses made prior to the correct identification included microvascular cranial nerve palsies in 3 patients. Sinus disease, “lazy eye,” and multiple sclerosis were each diagnosed in 2 patients. Other initial diagnoses included myasthenia, thyroid disease, labyrinthitis, trigeminal neuralgia, migraine, hypothyroidism, and “nerves.” Twenty-one patients (37%) had previous surgery.

TABLE 1. DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
1	11/07/87	58/F	12/29/87	Diplopia in L gaze, horizontal and oblique	Partial L VI	CT: enhanced fullness of L cavernous sinus. MRI: confirms mass in L cavernous sinus extending posteriorly—probable meningioma.	Compressive lesion involving L CN VI vs myasthenia gravis		Incomplete ophthalmoplegia OS with pupil sparing. Complete recovery of III with persistent V; late muscle surgery.
2	11/08/88	38/F	11/07/88	Horizontal, binocular diplopia increase in L gaze. History of intracavernous meningioma 10 years prior presenting with amenorrhea and galactorrhea.	Partial L VI & III and partial optic neuropathy	MRI: large tumor extension involving skull base, L cavernous sinus, L temporal fossa, and suprasellar region	Prolactinoma	✓	Complete left optic neuropathy and complete left ophthalmoplegia; late recovery of III with aberrant regeneration and neurotrophic keratitis.
3	04/26/89	41/F	04/24/89	Intermittent diplopia	Partial V, partial R VI	MRI: R cavernous sinus mass—probable meningioma	Meningioma		Complete ophthalmoplegia with late pupil-sparing and Horner's syndrome with late incomplete resolution and neurotrophic keratitis.
4	07/17/89	39/F	07/28/89	Throbbing, severe, retro-orbital L eye pain	Optic neuropathy	CT: mass extending from L posterior fossa through the L cavernous sinus, into the L anterior fossa	Meningioma		Partial L III palsy, decreased sensation over V, and a persistent L optic neuropathy. Complete resolution of III palsy, but severe neurotrophic keratitis treated with a Gunderson flap.
5	07/18/89	61/M	07/25/89	Binocular, vertical diplopia, prominence of OD, and ptosis OD. History of papillary carcinoma of the thyroid S/P thyriodectomy with residual R Horner's. History of episode of diplopia 4 years previously while hypothyroid—resolved after increased synthroid.	Partial R III with pupil-sparing, partial R VI, old R Horner's	CT/MRI: R parasellar mass consistent with meningioma	Hypothyroidism		Postop incomplete ophthalmoplegia OD and decreased facial sensation on L and partial optic neuropathy. 8 months out had some recovery of both III and VI function, but residual decreased sensation over VI. Persistent afferent pupillary defect, and arcuate visual field changes.

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
6	07/20/89	37/M	12/21/86	Diplopia, worse in L gaze. Auditory hallucinations in L ear.	Partial L VI	CT: L cavernous sinus mass—probable meningioma	Meningioma	✓	Complete left ophthalmoplegia with reported recovery of III nerve function but no recovery of left transected VI nerve. Left optic neuropathy with arcuate visual field defect, but relatively preserved central visual function.
7	08/11/89	58/F	08/12/89	Nausea, vomiting, diarrhea, grand mal seizure	None	CT: R sphenoid meningioma with associated R cerebral edema and mild to moderate midline shift	Meningioma		Incomplete R pupil-sparing III nerve palsy which cleared within 2 mo; mild facial numbness also cleared.
8	11/10/89	38/F	11/09/89	Bitemporal, daily headache; "eye strain"	Partial III nerve palsy, homonymous hemianopsia	CT: large L cavernous sinus mass	Meningioma		Postoperative R III and VI and L hemiparesis. Homonymous hemianopsia improved. Complete clearing of ophthalmoplegia.
9	11/14/89	39/F	09/03/87	Left upper lid ptosis and swelling L intermittent forehead pain	Partial III and partial optic neuropathy	CT: meningioma medial L middle cranial fossa	L optic neuropathy of unknown etiology	✓	Persistent L optic neuropathy, complete ophthalmoplegia except for incomplete abduction deficit. Late tumor regrowth with orbital roof involvement and persistent facial pain
10	01/17/90	48/M	01/13/90	Right upper lid swelling and intermittent horizontal diplopia	R III	CT/MRI: R parasellar mass involving the lateral wall of the cavernous sinus	Meningioma		Complete III, IV, and V cranial nerve palsies

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
11	04/09/90	65/F	03/08/90	History R temporal meningioma diagnosed in 1959 presenting with bifrontal headaches and seizures; S/P excision with resolution of symptoms. Seizure recurrence in 9/89.	None	CT: tumor involving the floor of the middle cranial fossa and R cavernous sinus	Meningioma	✓	Incomplete R optic neuropathy and almost complete ophthalmoplegia, sparing some abduction. Late development of aberrant regeneration.
12	04/10/90	46/F	04/08/90	Bilateral, perioral numbness. Severe weakness in R leg 3 yr later. Progressive hearing loss on L 9 yr later. Onset of loss of balance and diffuse weakness.	None	MRI: L CPA mass	Multiple sclerosis		Partial pupil-sparing III nerve palsy and complete VI nerve palsy. The III had cleared in 1 yr She underwent muscle surgery for residual V nerve palsy.
13	04/11/90	56/F	07/14/87	Episodic horizontal diplopia	Partial L VI and III, and almost complete V	CT: enhancing lesion in the CPA on the L	Microvascular CN VI palsy	✓	Complete L, pupil-sparing III, with complete V and partial VI. Initial improvement in III but with recurrent tumor growth, worsened III and VI. Developed neurotrophic keratitis.
14	04/12/90	61/F	04/11/90	Bifrontal headache. 11 yr later vertigo, vomiting, headache. 25 yr later swelling OS. 2 yr later swelling, diplopia, and blurred VA OS.	Partial L III	CT: L cavernous sinus mass	Sinusitis/ labyrinthitis		Complete ophthalmoplegia OS. Aberrant regeneration of III, but recovery of L VI and IV. Late progressive optic neuropathy due to recurrent tumor.
15	04/13/90	47/F	04/12/90	3-mo History L cheek pain, like a toothache; S/P sinus surgery	None	MRI: lesion extending along CN V behind tentorium	Sinusitis		L pupil-sparing III and partial L VI; III cleared by 4 mo, VI cleared by 2 wk

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
16	06/18/90	29/F	06/15/90	Decreased VA OD while 5 mo pregnant; at 7 mo developed dilated pupil OD; negative angiogram; resolution after delivery. Recurrence 15 mo later when again 5 mo pregnant; negative CT. Symptoms resolved after delivery. Recurrence 1 year later; positive CT	Mild R III with complete optic neuropathy	CT 3/85: with contrast. Mass involving cavernous sinus.	Meningioma		Complete ophthalmoplegia and transient hemiparesis
17	06/19/90	49/M	06/18/90	Horizontal, binocular diplopia headache	Partial L VI	CT: L cavernous sinus tumor	L cavernous sinus mass	✓	Persistent complete VI. Complete ophthalmoplegia with partial clearing of III with aberrant regeneration.
18	10/09/90	54/F	10/08/90	Severe bitemporal/occipital headaches associated with bending over, straining, coughing, valsalva, etc. These headaches differ from her long-standing tension headaches.	L IV and partial L V	CT: posterior fossa enhancing lesion with extension into middle fossa. MRI: large mass at clivus just deep to the CPA and left of midline extending to involve the L parasellar region.	Posterior fossa mass	✓	Complete ophthalmoplegia, partial III recovery with aberrant regeneration, development of severe neurotrophic keratitis. Treated with muscle surgery and tarsorrhaphy.
19	10/11/90	27/M	10/10/90	Daily, severe, pounding, occipital headaches associated with strenuous activity and changing position	Partial V, VI	CT: large cranial mass consistent with meningioma	Meningioma	✓	Complete ophthalmoplegia
20	01/28/91	23/F	01/24/91	Fell off a bicycle; later decreased VA OS	Complete L optic neuropathy	MRI: tumor involving L optic nerve by report	Optic neuritis	✓	Complete ophthalmoplegia III cleared within wk, VI cleared by 4 mo, mild residual V dysfunction, no improvement in optic nerve dysfunction

TABLE 1 (continued).. DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
21	01/30/91	51/M	01/28/91	History of frontal lobe meningioma Diagnosis in 1983, presented with headache and progressive dimming of VA; S/P resection in 1984. In 1987 noticed L facial numbness. Finally seen by a physician in 1990	Partial III and bilateral optic neuropathies	CT: initially read as negative. MRI: cavernous sinus tumor.	Cavernous sinus lesion	✓	Complete ophthalmoplegia with partial V and continued bilateral optic neuropathies
22	01/31/91	56/F	01/29/91	Binocular, vertical diplopia	L VI	MRI: large L parasellar tumor measuring 25×20×15 cm encasing the carotid, invading the cavernous sinus, and extending posteriorly to compress the pons	Meningioma		Complete ophthalmoplegia, L optic neuropathy with preserved central vision, partial clearing of III with aberrant regeneration, mild clearing of VI with persistent esodeviation. Treated with Faden procedure to expand BSV.
23	04/17/91	71/F	04/16/91	Short-term memory loss. Pain and numbness in her face.	None	CT: R clival mass	Meningioma		R complete III, partial R VI, partial V
24	04/18/91	79/M	04/08/91	Diplopia, worse on L gaze, better on R gaze	Partial III with pupil-sparing	MRI: R cavernous sinus mass	Meningioma		Partial pupil sparing III and complete VI, probable Horner's; by 4 mo complete clearing of VI, III partial recovery
25	04/19/91	45/F	05/19/88	Ptosis OS, progressive	Partial III with pupillary involvement. Superior division > inferior division.	CT: 2×2-cm enhancing mass centered around L anterior clinoid consistent with meningioma. MRI: L parasellar mass displacing the medial temporal lobe laterally and the carotid inferiorly and medially.	Meningioma	✓	Complete ophthalmoplegia homonymous hemianopsia related to CVA during carotid reanastomosis. No clearing.

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
26	04/28/91	48/F	01/29/91	Binocular horizontal diplopia	Complete L VI	MRI: mass in the L posterior cavernous sinus	Meningioma		Complete ophthalmoplegia with partial V. Incomplete recovery III and VI.
27	07/31/91	49/M	07/06/89	Intermittent ptosis OD. Vision "not quite right" OD × 3 yr. Recent onset proptosis OD.	R optic neuropathy, VI	CT and MRI: large lateral sphenoid wing mass typical of meningioma	Meningioma	✓	Persistent optic neuropathy with improved optic nerve function late and complete ophthalmoplegia with partial clearing within 3 mo and stabilization
28	08/26/91	46/M	08/22/91	History cluster headaches, normal CT × 3 years; difficulty fusing	None	MRI: CPA tumor	Acoustic neurilemoma	✓	Incomplete pupil sparing III, complete VI and V with exposure problems
29	08/27/91	57/F	02/21/89	History of L middle cranial fossa meningioma. Presented with headaches and L optic neuropathy in 1989. S/P near total resection in 12/89. In 6/91 complained of 2 months of decreased VA OS and increased proptosis and pressure OS.	Partial L V, optic neuropathy	MRI: extensive recurrence of meningioma in the L sphenoid wing, infratemporal fossa, L orbit, and L sphenoid and maxillary sinuses and ethmoid air cells	Meningioma	✓	Worsen L optic neuropathy, almost complete pupil-sparing III, complete V and VI. Almost complete clearing III by 2 mo and complete clearing by 5 mo of both V and VI. Persistent V with development of neurotrophic keratitis.
30	08/30/91	47/M	08/29/91	Could not focus OS. "VA to the L side was all haze."	Mild L optic neuropathy	CT: L cavernous sinus mass extending to the L side of the pituitary and anteriorly to the orbital apex. MRI confirmed and showed extension along the supracavernous portion of the L carotid.	Meningioma		Complete L ophthalmoplegia with absent corneal sensation and complete optic neuropathy

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
31	10/29/91	42/F	10/27/91	Fuzzy VA OD; 4 mo later proptosis OD; 6 mo later R-sided teeth and jaw soreness as well as progressive decreased VA OD and soreness OD	R optic neuropathy, partial III	CT (1/86): negative. MRI (6/86): negative. CT (9/97): R sphenoid wing meningioma	Thyroid orbitopathy/ sinusitis		Possible slight improvement in optic nerve function with decreased APD and improved visual fields. Persistent, incomplete III, minimal VI.
32	10/31/91	61/M	10/29/91	Binocular, horizontal diplopia	Complete R VI	MRI & CT: cavernous sinus mass	Meningioma		Complete ophthalmoplegia OD postoperative with good corneal sensation. 6 mo out had complete recovery of III, but still complete IV and VI palsies. Treated with botulinum toxin. Stable in 4/94.
33	11/06/91	56/F	11/05/91	Progressive ptosis OS	Pupil-sparing III, partial VI, L optic neuropathy	CT & MRI: cavernous sinus meningioma	Possible myasthenia gravis		Complete ophthalmoplegia OS with decreased corneal sensation, complete optic neuropathy
34	02/03/92	44/F	01/30/92	Continuous bifrontal pressure sensation	None	CT: left clival tumor	Meningioma		Partial pupil sparing III and complete VI, partial V dysfunction. Developed neurotrophic keratitis associated with VII dysfunction
35	02/04/92	28/M	01/31/92	Grand mal seizure while sleeping	None	CT: skull base tumor	Meningioma	✓	Partial pupil-sparing III and partial V and VI
36	02/06/92	67/F	02/05/92	Horizontal diplopia, progressive ptosis	Complete L VI, partial L III with pupillary involvement	MRI: retro-orbital tumor on the L	"Lazy eye"		Complete L ophthalmoplegia. Postoperative course complicated by aspiration pneumonia and death.

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
37	04/06/92	55/F	03/26/92	"Spells" associated with urinary incontinence 3 yr later progressive decreased VA OS	L optic neuropathy	CT/MRI: mass involving the medial aspect of the temporal lobe, the L parasellar region, and the L cavernous sinus	"Nerves"		Persistent L optic neuropathy with late improvement in APD, complete ophthalmoplegia with partial clearing with aberrant regeneration treated with muscle surgery
38	04/08/92	64/F	04/10/92	Horizontal diplopia for 1 yr. Having problems "falling out."	Mild III and VI	MRI: routine follow-up of petroclival meningioma	Meningioma	✓	Mild III nerve palsy with pupil-sparing and moderate VI nerve palsy with rapid clearing
39	04/09/92	57/F	10/22/87	Light-headedness and blurred vision followed by onset of binocular horizontal diplopia, worse in L gaze, history of severe hypertension	Partial L VI	CT: Normal. MRI (4.25 yr later): enhancing mass centered in Meckel's cave extending slightly inferiorly along the side of the clivus and medially into the middle cranial fossa	Microvascular VI palsy		Incomplete pupil sparing III, persistent incomplete VI; III cleared within 6 weeks, VI improved to better than preoperative
40	05/03/92	67/F	04/30/92	Horizontal diplopia at distance. Worse in R gaze.	Partial R VI	MRI: R cavernous sinus mass. Angiography: R cavernous sinus mass encasing the carotid artery	Partial R VI		Complete ophthalmoplegia OD
41	05/06/92	63/F	05/05/92	Loss of balance/ weak legs ×11 mo, AM bifrontal headaches, daily ×1 yr, falling episodes ×1 mo	None	CT: R CPA tumor	Meningioma		Partial R pupil sparing III, partial V

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
42	05/07/92	60/M	05/06/92	Vertical, binocular diplopia; 4 yr later L facial pain and decreased VA OS	Complete L VI, partial L III, L optic neuropathy	CT (87): negative. CT (11/91): "not definitive." MRI (12/91): L cavernous sinus mass	Meningioma		Complete ophthalmoplegia, V with loss of corneal sensation OS. Persistent optic neuropathy postoperative but decreased APD.
43	11/03/92	47/F	11/02/92	Spells: "all of the sudden it was like I had no brain, I was like a mushroom; I just felt dumb." Previous sphenoid wing meningioma	L optic neuropathy	MRI: mass in the cavernous sinus surrounding the carotid artery	Meningioma		L VI, incomplete, pupil sparing III, partial V
44	11/03/92	26/F	10/27/92	H/A ×6 mo; R facial droop; dizziness; blurred VA OD ×1 wk	R V	MRI: large mass at cranial base extending to R temporal fossa and pontocerebellar region with moderate hydrocephalus	Meningioma	✓	Complete R ophthalmoplegia, thalamic infarct
45	11/04/92	58/F	04/11/90	Transient blurry VA OS, 5-6 episodes per day	Complete L optic neuropathy, partial VI	CT: thickening of the optic nerve OS suggestive of a L optic nerve sheath meningioma	Meningioma		Complete L ophthalmoplegia, partial recovery III with aberrant regeneration, partial VI, persistent complete optic neuropathy
46	11/05/92	57/F	10/28/91	Severe R-sided and back of the neck headache sometimes assoc with nausea and vomiting. Also progressive loss of vision OD for 3 yr	R optic neuropathy	CT: tumor involving R cavernous sinus extending to orbital apex	Meningioma		Persistent optic neuropathy with improvement in APD. Complete ophthalmoplegia with partial clearing of III and complete clearing of VI.

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
47	02/14/93	81/M	02/04/93	7-mo History of recurrent double vision	Complete III, VI, incomplete V	MRI: recurrent growth in the cavernous sinus	Meningioma	✓	Persistent complete III, VI, but sparing IV, worsening V
48	04/22/93	45/M	04/20/93	Vertical diplopia and ear ache	Partial L III with pupil involvement	MRI: L cavernous sinus mass	Labyrinthitis		Complete L ophthalmoplegia, V, partial recovery III and VI. Development of neurotrophic keratitis.
49	04/23/93	73/F	04/20/93	S/P partial resection sphenoid ridge meningioma 1984 (originally presented w/eye swelling ×6 mo). Now with pressure sensation, decreased VA, and intermittent diplopia	R optic neuropathy	MRI and CT: increased growth of meningioma	Meningioma	✓	Persistent optic neuropathy, complete III, IV, and V, and incomplete VI. Parietal lobe infarction with left hemiparesis and homonymous hemianopsia.
50	04/29/93	32/F	04/27/93	Binocular, horizontal diplopia, worse in L gaze	L VI; partial III	MRI: L cavernous sinus mass	"Lazy eye"		Complete ophthalmoplegia with incomplete recovery by 3 mo, complete V with neurotrophic keratitis, treated with lubrication and tarsorrhaphy
51	06/03/93	55/F	06/03/93	Abnormal sensory perceptions over L face and inside of nose, mouth, eyelid, and ear canal; 6 mo later horizontal diplopia	Partial L VI	MRI: L parasellar mass affecting the cavernous sinus and likely the medial aspect of Meckel's cave	"This sometimes happens"		Complete ophthalmoplegia, partial V, temporal tip atrophy
52	06/04/93	51/F	06/01/93	1 yr History horizontal vision, dizziness and gait disturbance	Partial L V & VII	MRI: L cavernous sinus mass	"Headache"		Complete ophthalmoplegia, partial recovery of III with aberrant regeneration. Treated with muscle surgery. Complete V with neurotrophic keratitis treated with hard palate graft.

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
53	04/18/94	58/F	04/20/94	Pain & tingling in left side of nose radiating to left jaw and teeth ×1 wk	Partial V and VI	CT: reportedly negative. MRI: enhancing mass in the anterior aspect of Meckel's cave and the base of the middle cranial fossa compatible with a meningioma.	Trigeminal neuralgia		Partial pupil sparing III, cleared by 2 mo. Persistent V with slight late improvement. Persistent partial VI improved compared to preoperative.
54	04/19/94	50/F	04/17/94	Problems with hearing and balance	Complete R V, VI, and VII	MRI: recurrent tumor in the area of previous CPA tumor with extension to the cavernous sinus	Meningioma	✓	Incomplete pupil sparing III, persistent complete V, and worsening of preoperative VI
55	06/01/95	59/F	05/31/95	Intermittent pain OD, progressive bulging OD, one episode of diplopia lasting 1 mo	None	MRI/CT: intraosseous meningioma of R sphenoid wing with extension into the cavernous sinus on the R side	Meningioma		Complete ophthalmoplegia OD with absent corneal sensation

TABLE 1 (continued). DETAILS OF PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	DOS	AGE/SEX	IV	PRESENTING COMPLAINT	PREOPERATIVE CN PALSIES	IMAGING STUDIES	ORIGINAL DIAGNOSIS	PREVIOUS SURGERY	POST-INTERVENTION OUTCOME
56	06/02/95	39/M	06/01/95	Decreased VA	R optic neuropathy	MRI: medial sphenoid wing meningioma with carotid compression	Meningioma	✓	Complete ophthalmoplegia CSF leak
57	06/03/98	46/M	05/20/94	Difficulty picking things up with R hand and arm, paresthesias, mild R facial weakness	Partial L V, optic neuropathy	MRI: mass arising from the L posterior clinoid	Meningioma		Incomplete L pupil-sparing III almost cleared by 3 mo, complete L VI with moderate clearing by 3 mo, complete V with no improvement and development of neurotrophic keratitis

APD, afferent papillary defect; BSV, binocular single vision; CN, cranial nerve; CPA, cerebellar pontine angle; CSF, cerebral spinal fluid; CT, computed tomography; DOS, date of service; Dx, diagnosis; F, female; Hx, history; IV, initial visit; L, left; M, male; MRI, magnetic resonance imaging; OD, right eye; OS, left eye; Postop, postoperative; R, right; S/P, status post; Sx, symptoms; VA, visual acuity.

Presenting Complaints

At the time of presentation there was a history of double vision in 24 (42%) of 57 patients. The second most common symptom was headache or facial pain in 22 cases (39%). On the other hand, those patients presenting with headache were more likely to have a non-meningiomatous lesion (40% [10 of 25]) than meningiomas (19% [11 of 57]). Decreased or blurred vision occurred in 12 (21%) patients with meningiomas. Facial numbness was less common with meningiomas (7% [4 of 57]) than other pathology (16% [4 of 25]). Interestingly, 9 patients (16%) complained of problems with balance**,** light-headedness**,** or vertigo, 5 (9%) had seizures as their initial manifestation, and 4 (7%) had proptosis. Six patients (11%) noticed ptosis without double vision. Other complaints included memory loss, facial droop, amenorrhea, and weight loss. The distribution of symptoms in this series is similar to that of larger surgical series reported during the last 14 years (Table 2). It is interesting that previous literature has suggested that meningiomas do not produce pain,[109] yet headache and facial pain was, if not the most common, then the second most common symptom.

TABLE 2. SYMPTOMS OF CAVERNOUS SINUS PATHOLOGY IN CURRENT STUDY AND LITERATURE

SYMPTOMS	STUDY				MENINGIOMA	NONMENINGIOMA
	DOLENC[98]	SEPEHRNIA[120]	KIM[138]	CURRENT		
Headache	27 (43%)	35 (50%)	12 (57%)	21 (26%)	11 (19%)	10 (40%)
Decreased vision		28 (39%)	9 (43%)	19 (23%)	14 (25%)	5 (20%)
Amaurosis		11 (15%)				
Double vision	25 (40%)	17 (24%)	8 (38%)	41 (50%)	23 (40%)	18 (72%)
Ophthalmoplegia	3 (5%)		14 (67%)			
Exophthalmos	17 (27%)	11 (15%)		5 (6%)		
Pain	5 (8%)			16 (20%)	12 (21%)	4 (16%)
Sensory loss			7 (30%)	7 (9%)	3 (5%)	4 (16%)
Hemiparesis		6 (8%)				
Mental changes		4 (6%)		1 (1%)		
Epilepsy			5 (24%)	6 (7%)		
Other				28 (34%)		
No. of patients	63	71	21	82		

*Some patients had more than one symptom.

Postoperative Evaluation

All but one patient were seen immediately following surgery. Long-term follow up was not possible in all patients given that many were international. In addition, 2 patients succumbed to complications within 2 months**.** Thirty-two of the original 82 cases were re-evaluated 3 months or more following surgery (range, 3-228 months; mean 54.9 months) and were defined as the long-term follow-up group. Testing was modified to maximize the ability to compare function from the preoperative and immediate postoperative assessment. Quantitative pupillary assessment (neutral density filters[110]) and automated static perimetry were particularly helpful in longitudinally evaluating optic nerve function. Corneal sensitivity was checked with an esthesiometer. Motility was recorded using 9-cardinal position external photography, and when possible Hess screen and binocular single-vision field testing were repeated. Hess screen evaluation was not possible in patients with severe optic nerve or corneal dysfunction and was not helpful in those patients with complete ophthalmoplegia. A total of 27 of the 32 long-term patients were followed up with sequential Hess screen evaluation.

SURGICAL APPROACH

The surgery was done under the direction of a single senior skull base surgeon. This surgeon previously had, and continues to have, the largest personal series of cavernous sinus procedures. Although there were technical modifications during the series, the basic approach was similar throughout.[44,111,112] The surgery was performed using a combined intradural/extradural technique, including a pterional craniotomy and a microscopic approach to the cavernous sinus itself. This requires appropriate positioning and the use of a microscope. Three-point fixation of the head with a rotation 35° to the side is usually adequate to access the area of the pterion. Scalp incisions were usually coronal or less commonly bicoronal. The scalp was pealed forward. The temporalis muscle was mobilized superiorly, permitting a relatively low approach.

Other surgeons routinely remove the zygomatic arch, thus making this approach into an orbitozygomatic pterional one.[102,113,114]

This was believed to be unnecessary in this series. A single burr hole was placed just behind the superior portion of the lateral orbital rim. This ideally entered the orbit as well as the anterior cranial fossa. A second burr hole was placed posteriorly in the temporal region. The dura was freed from the overlying bone, and a pterional-based bone flap was raised, which permitted immediate view of the dura of both the anterior and middle cranial fossae.

An extradural dissection was then carried down to the foramen spinosum, where the middle meningeal artery was identified and ligated. Dissection was carried forward, while identifying the foramen ovale and the foramen rotundum anteriorly, all extradurally. The course of the intrapetrous carotid artery was also identified. The carotid canal,[115] within the petrous bone, was opened by dividing the greater superficial petrosal nerve (to prevent traction on the facial nerve) and by carefully removing bone back to the posterior loop of the carotid artery. Other surgeons have used this portion of the carotid artery to base a bypass graft when carotid sacrifice is planned.[116-118]

One of the disadvantages of this approach is the loss of the greater superficial petrosal nerve, which results in decreased reflex tearing by interrupting the parasympathetic innervation to the lacrimal gland. Wright[119] has more recently advocated a longer saphenous vein bypass graft from the cervical carotid to the distal supraclinoid carotid to avoid sacrificing the greater superficial petrosal nerve. Other surgeons believe that the possible complications of carotid revascularization procedures (as part of cavernous sinus surgery) outweigh their potential usefulness in increasing resectability.[120] De Monte[121] has written that carotid sacrifice is rarely, if ever, indicated. In this series, although 1 carotid artery ruptured and required sacrifice and 2 carotids were oversewn, no attempts at revascularization were made.

The periorbita and the dura are dissected free from the orbital roof, which is then removed. The greater wing of the sphenoid (the lateral wall of the orbit) is also taken down with ronguers, back to the superior orbital fissure and the foramen rotundum (Figure 2). The anterior clinoid, which represents the terminal portion of the lesser wing of the sphenoid, is carefully hollowed out by using a high-speed drill with a diamond burr. The residual bony rim is removed with curettes. In a small percentage of patients, the anterior clinoid may be connected via a bony strut back to the middle clinoid,[43] which makes removal of the anterior clinoid difficult and potentially more dangerous to the surrounding structures, especially the underlying optic nerve and carotid artery. The optic strut, which separates the optic canal from the superior orbital fissure, is further removed with the aid of rongeurs and the drill. Because there is aeration of the anterior clinoids in a small percentage of patients, an opening can be made into the paranasal sinuses. To avoid cerebrospinal fluid (CSF) leak, it is imperative to completely close the potential opening, usually with muscle and fibrin glue. Despite these precautions, CSF leaks are common in cavernous sinus skull base surgery.

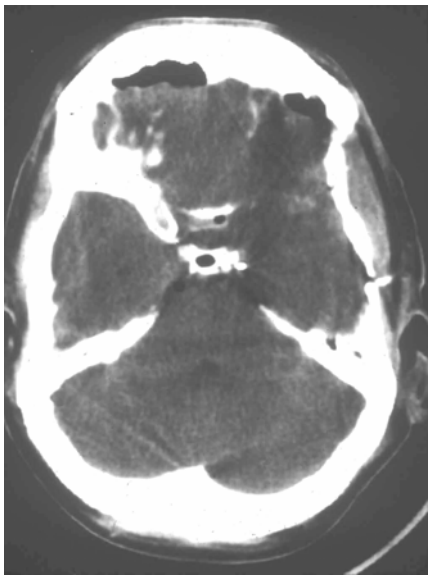

FIGURE 2

Case 30. Postoperative computed tomography scan following a pterional approach to the cavernous sinus. The roof and lateral wall, including the anterior clinoid, are gone on the left side.

Once the extradural portion of the operation is complete, the dura is opened. In the early cases in this series, the dura was opened inferiorly, thereby leaving a sheet of dura to protect the temporal lobe. A malleable retractor was then used to elevate the temporal lobe posteriorly and superiorly. Several of the early patients suffered detectable damage to the temporal lobe (infarct and secondary encephalomalacia) from long-duration compression by the static retractor. In later cases, a more medial approach was used by opening the Sylvian fissure, which permitted access to the lateral wall of the cavernous sinus without putting traction on the temporal lobe. In one case of a cavernoma, the cavernous sinus was entered without ever opening the dura by splitting the superior orbital fissure (following bony excision).

The direction of approach to the lesion within the cavernous sinus depends on the location of the tumor and its extent. In larger tumors that have secondarily invaded the cavernous sinus, often the tumor becomes obvious within the area of the middle cranial fossa or extends above the area of the cavernous sinus. When the tumor is small and localized, the cranial nerves, found within the lateral

wall of the cavernous sinus, must be identified to prevent direct damage. This is usually relatively easy with small lesions, but it may be more difficult when the tumors are larger and especially when they are infiltrative.

The earliest surgical opening into the cavernous sinus (in the modern era of skull base surgery) was via the potential space between the fourth cranial nerve above and the fifth cranial nerve below.[1] This triangular space has become known as Parkinson's triangle in honor of Dwight Parkinson, who initially described this surgical approach. The spaces between each of the cranial nerves also offer potential access to lesions within the cavernous sinus.[44] Another common approach is through the anterior cavernous roof. By removing the anterior clinoid, the space between the optic nerve and oculomotor nerve (the anteromedial triangle) opens directly into the anterior medial cavernous sinus.

Tumors often splay the cranial nerves apart, pointing the surgeon in the direction of easiest access. The various approaches have been enumerated by Dolenc in a series of named triangles. Surgery through each may be tailored to particular lesions, depending on their location. Other less common approaches to the cavernous sinus include a direct subtemporal approach to the lateral wall,[122] transmaxillary[123] or transfacial[124] access, and transphenoidal[125] and transnasal approaches.[126] Several of the latter involve endoscopy.[127] Lesions that extend into the posterior cranial fossa may require more extensive surgery (beyond the scope of this review). None of our patients required these alternative procedures.

One of the factors that prevented earlier surgical approach to cavernous sinus lesions was the fear of causing uncontrollable bleeding. The earliest surgery within the cavernous sinus was performed with patients under hypothermia and hypotensive anesthesia or even in cardiac arrest. Although bleeding still may present a challenge during surgery, this issue has turned out to be less of a problem than otherwise expected, given that the lesion itself displaces the venous space. Although there may be bleeding from the tumor, cavernous sinus bleeding per se is often not problematic until the tumor boundaries are reached. Surgical packing of the residual venous spaces usually controls blood within the surgical field. Several tumors in this series had residual bleeding despite the preoperative embolization, which was routinely performed. All of these instances were controlled intraoperatively.

RESULTS

MORBIDITY AND MORTALITY

Nonophthalmic complications of the cavernous sinus surgery in this series of 57 procedures included postoperative CSF leaks in 7. Most of these closed spontaneously. One patient required sacrifice of the carotid artery because of rupture during the procedure, and 5 patients had evidence of cortical infarction with resultant hemiparesis in 4 (transient in one). Additional nonophthalmic complications included one case of hydrocephalus, excessive bleeding resulting in premature termination of another case, and temporal lobe abscess in one patient. A pulmonary embolus was diagnosed in one patient while still hospitalized, and one patient had postoperative seizure activity. One patient developed aspiration pneumonia and succumbed to complications within 2 months of surgery.

OPTIC NERVE INVOLVEMENT

Twenty of the 57 patients with meningiomas had evidence of preoperative optic nerve dysfunction (Table 3). One patient had no perception of light perception (NLP), another had only hand motion vision, and one had 20/400 visual acuity. Two of these patients had previous surgery.

Five (25%) of the 20 patients showed immediate improvement, 8 (40%) experienced no change, and in 6 (30%) the dysfunction was worse postoperatively. The patient with NLP vision experienced no change. The patient with preoperative 20/400 vision could not be reassessed before leaving the hospital. Ten of the 20 patients with preoperative optic neuropathies underwent long-term follow-up (3 months or longer). Two of these (20%) had better central acuity than preoperatively, the neuropathy in 4 (40%) was the same, and 4 (40%) were worse than before surgery. Five patients (of 19 with preoperative optic neuropathies) had NLP (2 with short-term follow-up only), and the one patient preoperatively with NLP remained so. This was often anticipated preoperatively because tumor encased the optic nerve.

Thirty-seven patients had no evidence of preoperative optic nerve dysfunction. Thirty-three (88%) remained free of optic nerve dysfunction postoperatively, but four (11%) developed evidence of such dysfunction (Table 4). All 4 patients developed partial optic neuropathies with evidence of an afferent pupillary defect and visual field defects present on automated static perimetry (Figure 3). The field defects were characteristically arcuate in nature. There was relatively good preservation of central visual function in all 4 patients with new optic nerve dysfunction**.** There was marginally greater risk of a new optic neuropathy if the patient had previous surgery (2 of 14 [14%] without prior optic nerve damage) than if the patient had not had previous surgery (2 of 23 [8.7%]).

ABDUCENS NERVE INVOLVEMENT

Twenty-four of the 57 patients with meningiomas who underwent cavernous sinus surgery had preoperative evidence of sixth nerve dysfunction (Table 5). Six patients (11%) had complete abduction deficits preoperatively. Prior transcranial surgery did not seem to increase the risk of sixth nerve dysfunction. There was abnormal abduction in 42% of patients with previous cranial surgery (9 of 21) and 42% of patients without prior transcranial surgery (15 of 36). No patient with a sixth nerve palsy improved immediately following surgery, but 2 did clear later. All patients whose dysfunction was complete beforehand remained the same, and 12 (67%) of the remaining 18 patients (incomplete sixth nerve palsy preoperatively) progressed to a complete sixth nerve palsy immediately following surgery. Of the 9 patients who had evidence of abducens dysfunction and prior cavernous sinus surgery, one had complete

TABLE 3. PREOPERATIVE OPTIC NEUROPATHY IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	VISION	APD	VFD	BETTER	SAME	WORSE	VISION	APD	VFD	MISCELLANEOUS
2	✓	20/40	12	Severe constriction			✓	NLP	>3		
4		20/40	12	Inferior arcuate		✓		20/50	12	Inferior arcuate	Acuity lost to neurotrophic keratitis
9	✓	20/20	06	Inferior arcuate		✓		NLP	>3		Worse long term due to tumor progression, progressed to NLP
14		20/200	06	Central scotoma		✓		20/50	21	Central scotoma	APD greater, central visual function improved, late tumor regrowth. Worsened vision after 2nd surgery to 6/200.
16		NLP				✓		NLP			
21	✓	Hand motion; 20/200	06	Central Scotoma, nasal island		✓					
27	✓	20/40	12	Severe constriction		✓		20/50	09	Arcuate	Fields look better, expect artifact of field testing. Acuity & afferent same. Nice example of quantitative testing.
29	✓	20/25	06	Inferior arcuate			✓	20/40	12	Central scotoma	Eventually progressed to NLP due to progressive tumor
30		20/25	09	Moderate constriction			✓	NLP	>3		
31		20/30	21	Diffuse depression	✓			20/30	12	Improved still with arcuate	
33		20/100	18	Diffuse depression, increased blind spot			✓	NLP	>3		
37		20/30	15	Arcuate	✓			20/25	06	Arcuate	
41		20/25	03		✓				0		

TABLE 3(continued). PREOPERATIVE OPTIC NEUROPATHY IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	VISION	APD	VFD	BETTER	SAME	WORSE	VISION	APD	VFD	MISCELLANEOUS
42		20/70	21	Central scotoma	✓			20/100	09	Central scotoma	Decreased central acuity due to neurotrophic keratitis & severe motility problems. Without quantitation of pupils & perimetry patient would have been misclassified because his acuity was down.
43		20/70	06	Arcuate		✓					
45		20/20	3	Altitudinal field defect			✓	NLP	>3		Optic nerve sheath involvement
46		20/30	18	Diffuse depression	✓			20/50	12	Arcuate-improved	
49	✓	20/30	09	Diffuse depression		✓					
56	✓	20/400	18	Arcuate							
57		20/40	09	Central scotoma, arcuate			✓	20/200	21	Unable to perform automated perimetry	
TOTALS											
20					5	8	6				

APD, afferent papillary defect; NLP, no light perception; VFD, visual field defect.

dysfunction, and of the 8 with incomplete dysfunction, 5 progressed. Of the 9 patients with incomplete sixth nerve palsies who had not had prior surgery, 7 progressed. Thus prior surgery did not appear to put patients at increased risk for progression of a preexisting sixth nerve palsy.

TABLE 4. ACQUIRED OPTIC NERVE DAMAGE FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	ACUITY PREOP	ACUITY POSTOP	APD	VISUAL FIELD DEFECT	DIAGNOSING COMMENTS
5		20/25	20/40	09	Diffuse depression inferior arcuate	Without mild visual disturbance would probably have been missed
6	✓	20/15	20/50	12	Inferior arcuate	Would have been missed without detailed screening
11	✓	20/25	20/40	24	Severe constriction OD	Better central vision than field or afferent. Could have been missed.
22		20/20	20/25	09	Arcuate	Would not have been seen without fields

APD, afferent papillary defect; OD, right eye; Preop, preoperatively; Postop, postoperatively.

Long-term follow-up data were available in 16 of the original group of 24 patients with preexisting sixth nerve palsies. Seven remained complete, 7 were incomplete, and 2 recovered (Table 5). Neither of the patients who had long-term clearing of prior sixth nerve dysfunction had undergone transcranial surgery. Of the 6 patients with complete palsies preoperatively, long-term follow-up data were available in 4 cases, none of whom cleared.

Thirty-three patients had no evidence of an abduction deficit preoperatively. Twenty-five (76%) developed new sixth nerve palsies postoperatively (Table 6). Only 8 patients retained complete abduction immediately postoperatively. Only 2 (17%) of 12 patients who had previous transcranial surgery but no sixth nerve palsy preoperatively remained free of sixth nerve dysfunction, whereas 6 of 21 without prior surgery (29%) managed to have no evidence of abduction deficit postoperatively. Acute abduction deficits often improved. Only one patient with a surgically acquired sixth nerve palsy had no return of function with long-term follow-up. Seven patients with sixth nerve dysfunction preoperatively remained complete with long-term follow-up, including 3 whose defect was incomplete preoperatively. Seven of 25 patients with abducens palsies postoperatively recovered completely, but 6 retained incomplete abduction deficits. Five of 7 patients who recovered had experienced a complete deficit immediately postoperatively, and 2 had experienced an incomplete deficit. Combining the 2 groups at their last follow-up visit, only 9 (30%) of the 30 patients with long-term follow up were completely free of sixth nerve dysfunction, 8 (27%) had complete abduction defects, and 13 (43%) had partial dysfunction.

TROCHLEAR NERVE INVOLVEMENT

The fourth nerve function is the most difficult to analyze in this series. No patients had an isolated preoperative fourth nerve palsy, and only one patient had evidence of a combined fourth and third nerve palsy. In most patients who had evidence of fourth nerve dysfunction postoperatively, it occurred in the setting of complete ophthalmoplegia (38 of the 57 procedures). Two additional patients had evidence of superior oblique dysfunction without complete ophthalmoplegia. It was often difficult to tell whether the fourth nerve remained a clinical problem and was not seen as an isolated symptomatic deficit.

OCULOMOTOR NERVE INVOLVEMENT

Nineteen (33%) of the 57 cases had evidence of preoperative dysfunction of the third nerve (Table 7). Surprisingly, previous intracranial surgery did not increase the likelihood of third nerve dysfunction (29% [6/21] vs 36% [13/36]). These included one complete third nerve palsy and 18 incomplete third nerve palsies. Nine (47%) of the 19 had evidence of pupil involvement, whereas 10 (53%) had pupil sparing. Pupil sparing with slowly growing cavernous sinus lesions is not uncommon.

None of the 19 patients with preoperative third nerve palsies recovered immediately following surgery. The one patient with a complete third nerve palsy preoperatively remained so postoperatively, and an additional 15 patients progressed from incomplete to complete oculomotor paralysis. Prior transcranial surgery slightly increased the risk of progression from incomplete to complete. Five of 6 patients who had prior surgery and incomplete third nerve palsies progressed (83%), whereas 77% of patients without prior surgery had their third nerve palsy become complete (10 of 13). In the short-term postoperative analysis, 7 continued to have no evidence of pupillary involvement. An additional 6 (60%) of the previous 10 patients with no pupil involvement developed evidence of pupillary dysfunction.

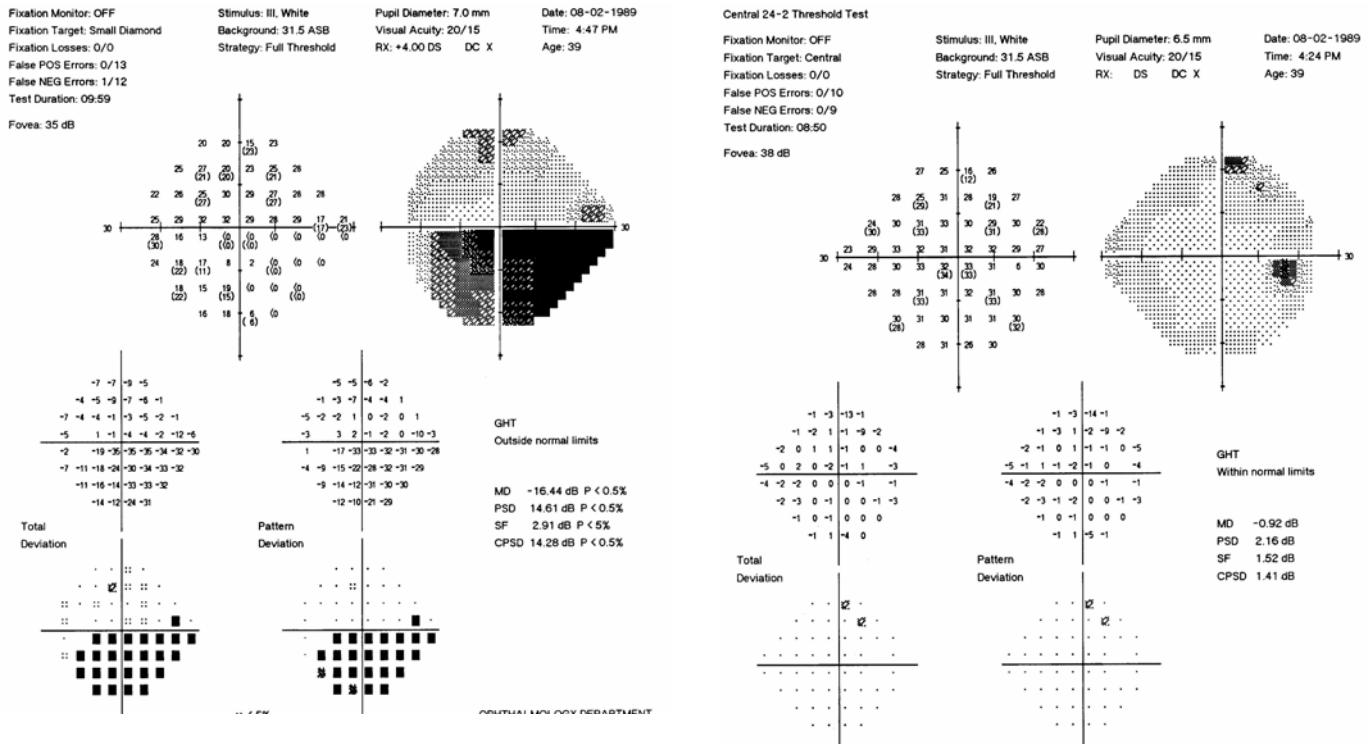

FIGURE 3

Case 6. Visual fields, left eye (left) and right eye (right), following resection of cavernous sinus tumor. In 1986, a 36-year-old patient was referred with intermittent double vision. At that time, he had evidence of a minimal abduction deficit OS, and a computed tomography scan revealed a mass within the left cavernous sinus. The double vision waxed and waned, but when it worsened in July 1989, he was reevaluated. At that time his afferent system was entirely normal, with 20/15 visual acuity, no evidence of an afferent pupillary defect, and normal visual fields. He had an abduction deficit OS, with 14 diopters of esodeviation in primary position. He was able to fuse in right gaze with normal stereopsis. Hess screen and binocular single-vision fields confirmed the presence of a left abduction deficit. On July 20, 1989, he underwent a pterional approach and cavernous sinus resection of a meningioma. During the procedure, the left sixth nerve, which went directly through the tumor, was transected and repaired. Postoperatively, he had complete ophthalmoplegia OS. He also had evidence of a new left afferent pupillary defect. Quantitative evaluation 2 weeks after surgery revealed visual acuity of 20/15 and 20/60 and a new 1.2 log unit left afferent pupillary defect and inferior arcuate field defect OS. By 5 months after surgery, his third nerve palsy had completely cleared, but he had a residual complete left sixth nerve palsy. His acuity OS remained good, but his inferior arcuate defect persisted (24-2 program).

Variable improvement tended to occur. We had long-term follow-up data in 12 of the 19 patients who had had preoperative third nerve palsies. None of these resolved completely, 8 partially resolved, and 4 had persistent complete third nerve paralysis. Three patients who had only experienced incomplete dysfunction preoperatively had complete third nerve palsies in the long term. No patients with preexisting oculomotor dysfunction showed improvement in their third nerve dysfunction There was evidence of pupillary dysfunction in 9 of the 12 patients with residual third nerve dysfunction, despite the partial recovery in the long term. In addition, 2 of the 8 patients with residual incomplete third nerve palsies developed aberrant regeneration. Both of these patients had undergone prior intracranial surgery.

Thirty-seven (97%) of the 38 patients who did not have a third nerve palsy preoperatively developed evidence of third nerve dysfunction postoperatively (Table 8). Only one patient with a meningioma postoperatively remained completely free of third nerve dysfunction. Of these new cases of third nerve dysfunction, 25 (68%) were complete and 12 (32%) were incomplete. Pupillary involvement broke down almost equally, with evidence of pupillary dysfunction in 19 but none in 18. There were long-term follow-up data in 23 patients in this subset. Thirteen cases (57%) cleared completely (Figure 4), and 10 (43%) cleared incompletely.

As an indication of the meticulous aspects of the cavernous dissection, no patient without oculomotor palsy preoperatively was left with a complete third nerve palsy, but 7 patients (37%) with incomplete defects did have evidence of aberrant regeneration (Figure 5).

TABLE 5. PREOPERATIVE SIXTH NERVE DYSFUNCTION IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	PREOP COMPLETE	PREOP INCOMPLETE	EARLY F/U COMP	EARLY F/U INCOMP	LONG-TERM F/U COMPLETE	LONG-TERM F/U INCOMPLETE	RECOVERED	TREATMENT	MISC
1			✓		✓		✓			
2	✓		✓	✓			✓			
3			✓	✓			✓			
5			✓	✓			✓			
6	✓		✓	✓						Transection of VI nerve w/attempted anastomosis
13	✓		✓		✓	✓				Due to tumor progression no worsening with surgery
17	✓	✓		✓		✓				
18	✓		✓	✓		✓			Muscle surgery with transposition	
19	✓		✓	✓						
24		✓		✓		✓				2nd operation
26			✓	✓				✓		Recovery from preop
27	✓		✓	✓			✓			
32		✓		✓		✓			Botulinum toxin injections	
33		✓		✓						
36		✓		✓						
38	✓		✓		✓					
40			✓	✓						
42		✓		✓		✓				
45			✓	✓			✓			

TABLE 5(continued). PREOPERATIVE SIXTH NERVE DYSFUNCTION IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	PREOP COMPLETE	PREOP INCOMPLETE	EARLY F/U COMP	EARLY F/U INCOMP	LONG-TERM F/U COMPLETE	LONG-TERM F/U INCOMPLETE	RECOVERED	TREATMENT	MISC
50			✓	✓			✓			
51			✓	✓						
52			✓	✓		✓			Muscle surgery with transposition	
53			✓		✓			✓		Better than preop
54	✓		✓		✓					
TOTALS										
24		6	18	19	4	7	7	2		

Comp, complete; F/U, follow-up; Incomp, incomplete; Misc, miscellaneous; Preop, preoperative.

TABLE 6. NEW SIXTH NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	ST COMP	ST INCOMP	LT COMP	LT INCOMP	RECOVERED	TREATMENT	MISCELLANEOUS
8			✓			✓		
9	✓		✓		✓			
11	✓		✓		✓			Some improvement
12		✓			✓		Muscle surgery	
14		✓				✓		Recovered within 6 mo
15			✓			✓		
16		✓						
20	✓	✓				✓		
21	✓	✓						
23			✓					
24		✓				✓		
25	✓	✓		✓				
29	✓	✓				✓		Partial clearing by 2 mo, complete by 5 mo
30		✓						

TABLE 6 (continued). NEW SIXTH NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	ST COMP	ST INCOMP	LT COMP	LT INCOMP	RECOVERED	TREATMENT	MISCELLANEOUS
31			✓					
34		✓						
35	✓		✓					
37		✓			✓			
43		✓						
44	✓	✓						
46		✓				✓		
48		✓			✓			
73	✓		✓					
55		✓			✓			
56	✓	✓						
TOTALS								
25	10	17	8	1	6	7		

Comp, complete; Incomp, incomplete; LT, long-term; ST, short-term.

TABLE 7. PREOPERATIVE THIRD NERVE DYSFUNCTION IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	PREOP COMPLETE	PREOP INCOMPLETE	SHORT-TERM COMPLETE	SHORT-TERM INCOMPLETE	LONG-TERM COMPLETE	LONG-TERM INCOMPLETE	RESOLVED	ABERRANT REGENERATION	MISCELLANEOUS
2	✓		PS	P			P		✓	
5			P	P			P			No worse than preop
8			PS		PS		PS			Some improvement
9	✓		P	P		P				
10			P	P						
13	✓		PS	PS			PS			Later developed
14			P	P			P		✓	
16			PS	P						
21	✓		PS	P						
24			PS		PS		PS			
25	✓		P	P		P				

TABLE 7(continued). PREOPERATIVE THIRD NERVE DYSFUNCTION IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	PREOP COMPLETE	PREOP INCOMPLETE	SHORT-TERM COMPLETE	SHORT-TERM INCOMPLETE	LONG-TERM COMPLETE	LONG-TERM INCOMPLETE	RESOLVED	ABERRANT REGENERATION	MISCELLANEOUS
31			P		P					
33			PS	P						
36			P	P						
38	✓		PS		PS					
42			PS	P		P				
47	✓	P		P		P				
48			P	P			P			
50			PS	P			P			
TOTALS										
19	7	P=1	P=8 PS=10	P=14 PS=1	P=1 PS=3	P=4	P=5 PS=3	0	2	

P, pupil; PS, pupil sparing.

TABLE 8. NEW THIRD NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	SHORT-TERM COMPLETE	SHORT-TERM INCOMPLETE	LONG-TERM COMPLETE	LONG-TERM INCOMPLETE	RECOVERED	ABERRANT REGENERATION	TREATMENT	MISCELLANEOUS
1		PS				✓			Cleared by 7 mo
3		PS				✓			
4			PS			✓			Cleared by 5 mo
6	✓	P				✓			Cleared by 3 mo
7			PS			✓			Cleared by 2 mo
11	✓	P			P		✓		
12			PS			✓			Cleared by 1 yr
15			PS			✓			Cleared by 4 mo
17	✓	P			P		✓		
18	✓	PS			PS		✓	Muscle	
19	✓	P							
20	✓	PS				✓			Cleared 1 wk

TABLE 8 (continued). NEW THIRD NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	SHORT-TERM COMPLETE	SHORT-TERM INCOMPLETE	LONG-TERM COMPLETE	LONG-TERM INCOMPLETE	RECOVERED	ABERRANT REGENERATION	TREATMENT	MISCELLANEOUS
22		P			P		✓	Muscle	
23		P							
26		P			P				
27	✓	P			P				Improving by 3 mo, no further clearing
29	✓		PS			✓			Cleared by 5 mo
30		P							
32		PS				✓			Cleared by 6 mo
34			PS						
35	✓		PS						
37		P			P		✓		
39		PS				✓			Cleared by 6 wk
40		P							
41			PS						
43			PS						
44	✓	P							
45		P			P		✓		
46		P			P				
49	✓	P							
51		P							

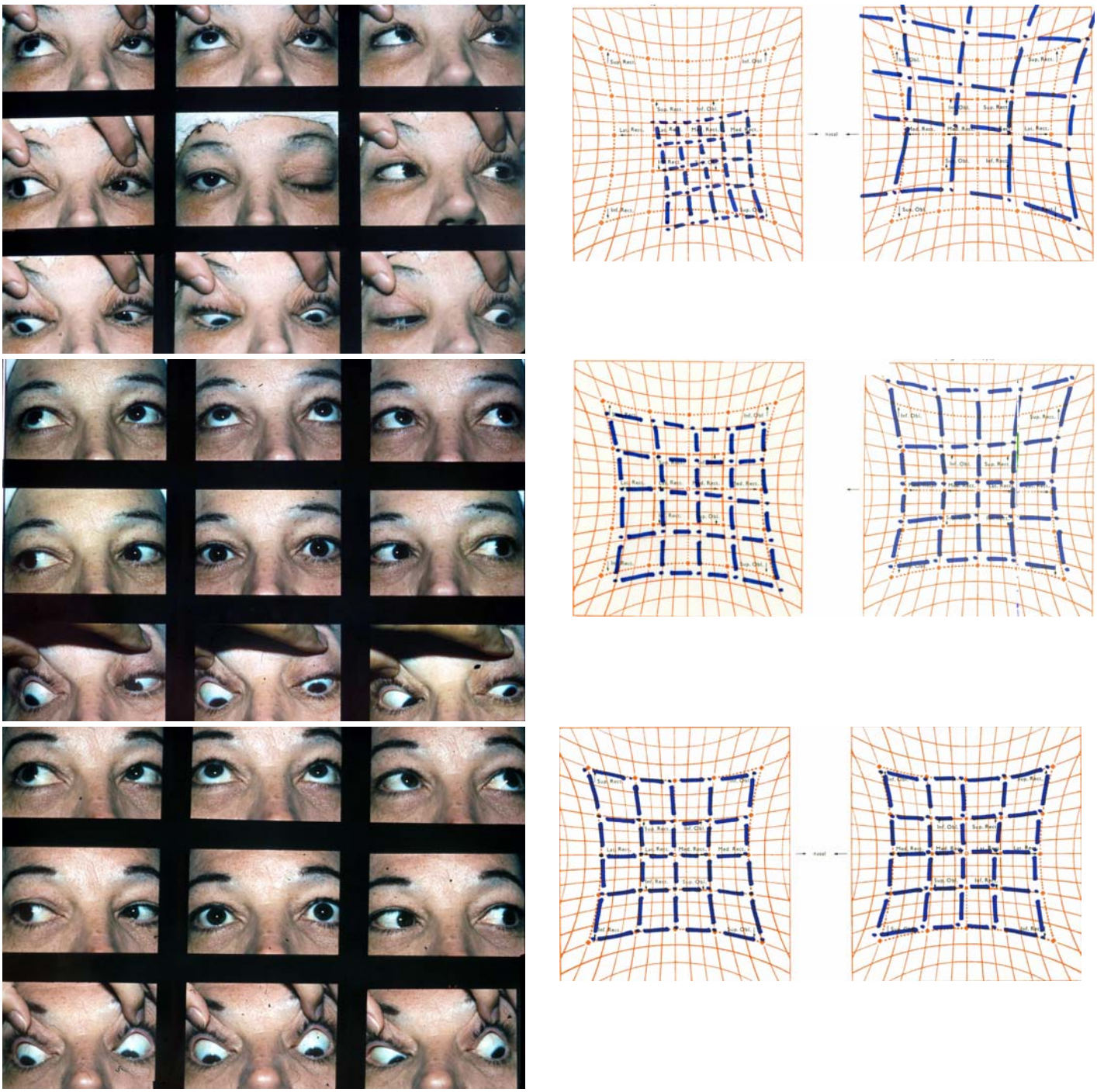

FIGURE 4

Case 15. A 47-year-old patient presented with a 3-month history of pain involving her left cheek. An otolaryngologist thought it was a sinus infection. She then saw 2 oral surgeons, who informed her that her symptoms were caused by her gums. A neurologist ordered an MRI scan, which revealed a mass involving Meckel's cave extending to involve the cavernous sinus on the left side. On April 15, 1990, she underwent a left pterional craniotomy with microdissection of the left cavernous sinus and removal of a meningioma involving Meckel's cave, the cavernous sinus, and the tentorium. Immediately postoperatively she was noted to have limitation in upgaze as well as abduction, indicating partial left third and sixth nerve palsies (row 1, left). Four days following surgery, Hess screen confirmed the incomplete left third and left sixth (row 1, right). Clinical examination showed gradual clearing. At 1 month she had minimal residual problems with upgaze OS (row 2, left), confirmed on Hess screen (row 2, right). At the 4-month follow-up examination, her cranial nerve palsies had cleared completely (row 3). Many patients clear their ophthalmoplegia rapidly. This is well illustrated on the Hess screen, which demonstrates the gradual clearing with each subsequent visit.

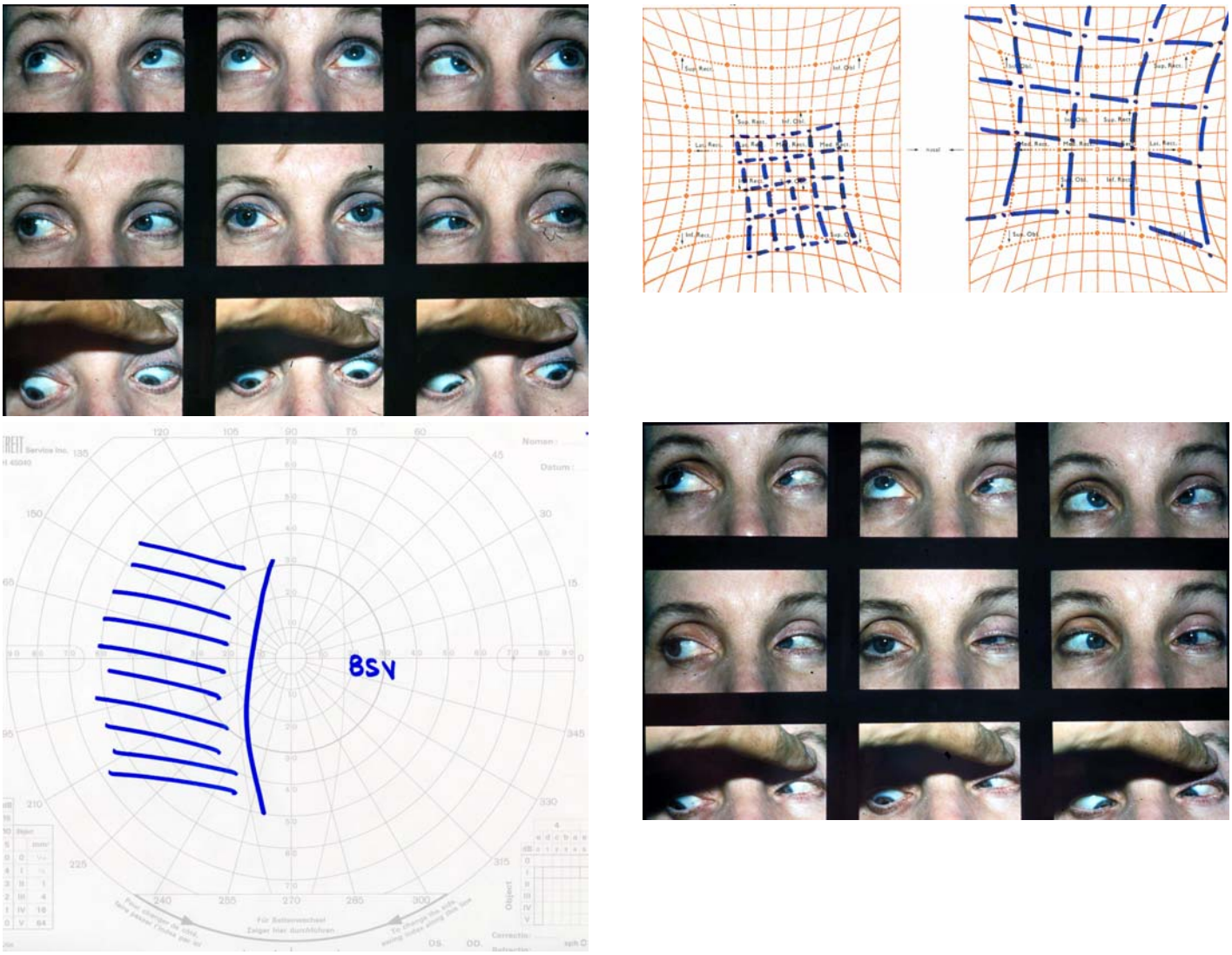

FIGURE 5

Case 52. A 51-year-old patient presented with a 1-year history of intermittent but progressive binocular diplopia. She noticed that this was worse on left gaze and was accompanied with gradually increasing pain on the left side of her face, involving the left temple and ear. Her internist arranged for an MRI scan, which demonstrated a mass in the left cavernous sinus. On preoperative evaluation her afferent system was entirely normal, and facial sensation was subjectively decreased over V1, V2, and V3 on the left side with a minimal decrease in corneal sensation (esthesiometer 6/5). She had evidence of abducting delay on the left side (top left) with 12 diopters of esodeviation. Slit-lamp examination, including the cornea, was otherwise unremarkable. Hess screen confirmed limitation in abduction on the left (top right), and binocular single vision fields confirmed diplopia on left gaze (bottom left). On June 4, 1993, she underwent a pterional craniotomy with resection of a left cavernous sinus meningioma. Immediately postoperatively she had complete ophthalmoplegia on the left with complete loss of corneal sensation. By 2 months she still had 7 mm of ptosis on the left side, but 4 mm upper lid range and early recovery of adduction and minimal vertical movements on the left side. By 4 months her cornea was still anesthetic. She had 2 mm of residual ptosis on the left side with a very large-angle esodeviation and inability to bring the left eye to midline (bottom right). (continued)

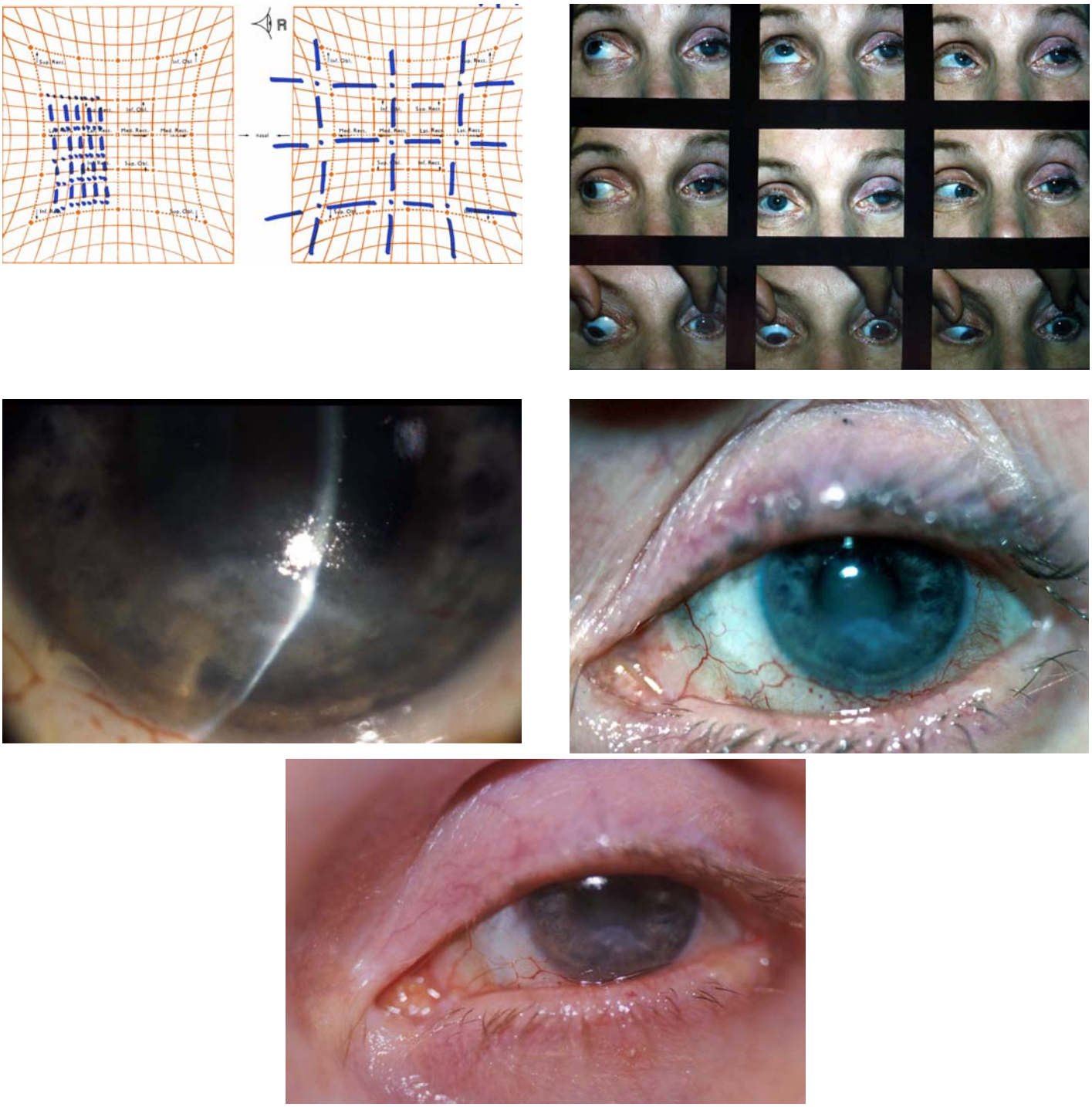

FIGURE 5 (continued)

She had evidence of lid elevation compatible with aberrant regeneration of the third nerve. Eight months following surgery she underwent a transposition procedure for persistent complete left sixth nerve palsy. This resulted in alignment of the left eye with a slight exodeviation and persistent limitation in vertical movement on the left best seen on her repeated Hess screen (top left). Four years later she had developed significant problems with inferior corneal exposure and recurrent epithelial breakdown related to the persistent anesthesia of the cornea (top right and middle left) and limited vertical movement (middle right). She underwent a hard palate graft in February 2000, elevating the left lower lid and decreasing the injection and epithelial irregularity (bottom). Neurotrophic keratitis occurred frequently in the setting of complete corneal anesthesia. Limitation in vertical movement also contributed. The cornea was protected by elevating the lower lid with the hard palate graft.

A total of 9 patients had aberrant regeneration of the third nerve, 2 with prior oculomotor deficits and 7 who developed third nerve

dysfunction postoperatively. Of the preexisting third nerve dysfunction, one case of aberrant regeneration developed in a patient with prior surgery, and the other had no prior history of intervention. Of the 7 cases in patients without a prior third dysfunction, 3 occurred in patients with prior surgery (3 of 13 [23%]) and 4 were in patients without surgery (4 of 24) [17%].

The chance of complete recovery was substantially better if the palsy was incomplete following surgery. Fifteen of 16 patients (94%) who had incomplete clearing immediately postoperatively and had long-term follow-up recovered. When the third nerve palsy was complete following surgery, only 6 (32%) of 19 cases recovered totally. No cases of new oculomotor dysfunction remained complete. Of the 10 cases improving but not clearing, 7 demonstrated evidence of aberrant regeneration. There did not seem to be an increased risk associated with prior surgery. Although 4 of 10 patients who did not clear completely had prior intracranial surgery, 6 did not, and 1 of the 6 patients who demonstrated complete clearing had prior surgery. Both patients who developed new complete third nerve palsies had not had previous surgery. Thus, although patients with immediate worsening of third nerve function postoperatively usually improved, this was not universal and definitely not always complete.

TRIGEMINAL NERVE INVOLVEMENT

Thirteen (23%) of 57 patients had preoperative evidence of trigeminal dysfunction (Table 9). Sensory loss was more common in patients who had undergone prior surgery (29% [6 of 21] vs 19% [7 of 36]). Two patients had no corneal sensation (most commonly related to previous surgery). Immediately following surgery, 4 of 11 cases that had incomplete sensory dysfunction remained incomplete, and 6 of the other 7 lost all corneal sensation. Only 1 patient (8%) experienced improvement. None of the patients with complete fifth nerve dysfunction demonstrated immediate improvement. Long-term follow-up data were available in 9 of the 13 patients who had preoperative trigeminal dysfunction. Six remained complete, 2 partially recovered, and 1 completely recovered.

Loss of corneal sensation was of considerable clinical significance. Only 1 of 7 preoperatively anesthetic patients partially recovered with long-term follow-up (representing functional improvement). Both patients with completely anesthetic corneas preoperatively developed neurotrophic keratitis. Four additional patients with partial anesthesia preoperatively developed neurotrophic keratitis after becoming completely anesthetic postoperatively.

Thirty-four (77%) of the 44 patients who did not have evidence of preoperative fifth nerve dysfunction developed evidence of postoperative hypesthesia (Table 10). The risk of developing a new trigeminal palsy was slightly greater if the patient had undergone previous transcranial surgery (87% [13 of 15] vs 72% [21/29]). Twenty-one of these newly affected patients (62%) were completely anesthetic, and 13 (38%) had decreased sensation. Long-term follow-up data in 19 of these 34 patients revealed recovery in 2, incomplete dysfunction in 7, and complete anesthesia in 10. Five of the 13 who acquired anesthesia improved to hypesthesia with long-term follow-up. Of the 2 who completely recovered, both were partially compromised postoperatively. Six (60%) of the 10 persistently anesthetic patients developed neurotrophic keratitis.

MISCELLANEOUS OPHTHALMIC COMPLICATIONS

Forty-seven additional complications occurred in 32 of the 82 procedures, including several ophthalmic complications. Horner's syndrome developed in 3 patients and homonymous hemianopsia in 4.

SUMMARY OF RESULTS

Patients undergoing cavernous sinus surgery can usually expect new ophthalmic complications together with an exacerbation of preexisting neuro-ophthalmic deficits. Although improvement in function can be achieved, it is distinctly uncommon. Worsening of ophthalmoplegia postoperatively appears to be the rule rather than the exception. Transient postoperative ocular motor palsy may improve especially if incomplete in the immediate postoperative phase. Aberrant regeneration of the third nerve is not uncommon, resulting in persistent motility problems. Worsening of optic nerve function may be underappreciated, especially if quantitative assessment is not performed. Trigeminal dysfunction may have a significant effect on visual function, especially if complete, as an anesthetic cornea is at high risk for development of neurotrophic keratitis.

DISCUSSION

OPTIC NEUROPATHY

The worsening of optic nerve function in patients who were previously compromised is likely a manifestation of the extent of the tumor as well as attempts at aggressive surgical removal. In at least 3 cases, the meningioma was preoperatively noted to extend completely around the optic nerve, thus ensuring loss of optic nerve function with complete resection. In these cases, the potential for visual loss was discussed with each patient.

A more interesting question involves those preoperatively normal patients who developed optic nerve dysfunction postoperatively. The mechanism is unclear. While it is possible vasospasm may play a role, the most likely culprit is direct damage at the time of the clinoid removal. In this series the clinoid was removed extradurally, which may increase the risk over an intradural approach. This has been noted, although not emphasized, in the literature. In a series of 40 patients undergoing clinoid removal, 31 of which were done extradurally, 3 patients suffered postoperative diminution of visual acuity or visual field.[128] None of the 9 patients in whom an intradural approach was used had similar complications.

TABLE 9. PREOPERATIVE FIFTH NERVE DYSFUNCTION IN PATIENTS UNDERGOING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	PREOP COMP	PREOP INCOMP	POSTOP COMP	POSTOP INCOMP	LATE F/U COMP	LATE F/U INCOMP	RECOVERED	NEUROTROPHIC KERATITIS	TREATMENT	MISC
3			✓	✓		✓			✓		
13	✓	✓		✓		✓			✓		
14			✓		✓			✓			
23			✓		✓						
24			✓	✓		✓					
27	✓		✓	✓			✓				
29	✓		✓	✓		✓			✓	Lubrication	Persistent facial pain
38	✓		✓		✓						
44	✓		✓	✓							
52			✓	✓		✓			✓	Hard palate	
53			✓		✓		✓				
54	✓	✓		✓					✓	Tarsorrhaphy	Facial nerve palsy
55			✓	✓		✓			✓	Aggressive lubrication	
TOTALS											
13		2	11	9	4	6	2	1	6		

Comp, complete; F/U, follow-up; Incomp, incomplete; Misc, miscellaneous; Preop, preoperative; Postop, postoperatively.

TABLE 10. NEW FIFTH NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	EARLY F/U COMP	EARLY F/U INCOMP	LONG-TERM F/U COMP	LONG-TERM F/U INCOMP	RECOVERED	NEUROTROPHIC KERATITIS	TREATMENT	MISCELLANEOUS
2	✓	✓		✓			✓	Tarsorrhaphy	
4		✓		✓			✓	Gunderson flap	
5		✓			✓				
6	✓	✓							
7			✓			✓			
9	✓	✓		✓					

TABLE 10 (continued). NEW FIFTH NERVE DYSFUNCTION FOLLOWING CAVERNOUS SINUS SURGERY

CASE	PREVIOUS SURGERY	EARLY F/U COMP	EARLY F/U INCOMP	LONG-TERM F/U COMP	LONG-TERM F/U INCOMP	RECOVERED	NEUROTROPHIC KERATITIS	TREATMENT	MISCELLANEOUS
10		✓							
11	✓	✓		✓					
15			✓			✓			
16		✓							
17	✓	✓			✓				
18	✓	✓		✓			✓	Tarsorrhaphy	
19	✓	✓							
20	✓		✓		✓				
21	✓		✓						
22		✓		✓					
25	✓	✓			✓				
26			✓		✓				
30		✓							
33			✓						
34			✓				✓	Patching	Facial nerve palsy
35	✓		✓						
37		✓		✓				Aggressive lubrication	
40		✓							
41			✓						
42		✓		✓					
43			✓						
45			✓		✓				
46			✓		✓				
48		✓		✓			✓	Aggressive lubrication	
49	✓	✓							

It is presumed that surgical manipulation around the optic nerve was responsible for the development of the optic nerve dysfunction in the 4 patients who developed partial but incomplete optic nerve damage. In particular, even the careful attempt to core the anterior clinoid with a high-speed drill puts the optic nerve at risk. There can be tremendous heat transfer with the use of a diamond burr (used to decrease bleeding and limit kickback in this tight space). Dolenc[44] specifically stressed the importance of adequate irrigation during drilling to minimize heat transfer. It is possible that significant temperature elevation occurred, despite the best efforts at continuous irrigation.

The incidence of new optic nerve damage in this case (7%) is substantially higher than that in previously reported series of cavernous sinus cases undergoing surgery. The easiest explanation for this incidence (not previously reported) is that without quantitative assessment of optic nerve function, these cases would likely have been missed clinically. Although the afferent pupillary defect ranged from 0.9 to 2.4 log units, central acuity was no worse than 20/50 in the 4 patients. Without measuring the afferent pupillary defect or obtaining quantitative perimetry for evidence of arcuate visual field defects, this dysfunction would have been overlooked. Thus, more careful attention to optic nerve function postoperatively may well detect unrecognized optic neuropathy.

ABDUCENS PALSY

A sixth cranial nerve palsy was the most common preoperative manifestation of cavernous sinus lesions in this series. None of the patients who had complete defects preoperatively recovered function, and although transient postoperative sixth nerve palsies did clear in a substantial portion of cases, only 9 of 30 (30%) were completely free of an abduction deficit when evaluated during a follow-up of 3 or more months postsurgery. Two patients (8%) with preoperative (all incomplete) sixth nerve palsies did recover normal function, but 13 (72%) of 18 had worse function than preoperatively, and all 6 who were complete preoperatively remained so Of the 33 patients without abducens palsies at the time of surgery, 25 (76%) developed an abduction deficit acutely. Although 50% of these cleared with long-term follow-up, 6 remained incomplete and 1 complete sixth nerve palsy failed to improve at all.

It has been suggested by neurosurgeons that an “easy muscle procedure will correct a patient with VI nerve palsy.” Although it is true that muscle surgery can be done to provide binocularity centrally and probably with at least some degree of eccentric gaze, patients with complete sixth nerve palsies are much more difficult to align, with a resultant much smaller binocular field.

TROCHLEAR PALSY

In this review of prior discussions of complications in cavernous sinus surgery, the most difficult data to sort out are those involving the fourth cranial nerve. The fourth nerve should be at the same risk of damage as the third nerve and the first division of the fifth nerve because it runs within the lateral wall of the cavernous sinus. In addition, the fourth nerve is often damaged because it runs under the tentorial edge, prior to entering the cavernous sinus. Any incision in the tentorial edge may result in fourth nerve dysfunction. Gordy[129] reported a transient fourth nerve palsy following the removal of a Gasserian neurilemoma. Most important, however, it is often very difficult to determine whether the fourth nerve is involved. In the setting of a complete third nerve palsy, preservation or loss of incyclotorsion with an attempted downward gaze will indicate whether the fourth nerve is functional. When the third nerve involvement is partial, however, fourth nerve function may be indeterminate. Previous reports of fourth nerve involvement must be viewed in light of this clinical difficulty.

OCULOMOTOR PALSY

A pupil-sparing third nerve palsy due to an aneurysm of the posterior communicating artery is extremely rare. With the slow progression of cavernous sinus pathology, sparing of the pupil is not unusual, as demonstrated in our preoperative evaluation. Less often, more rapidly growing parasellar lesions may also produce pupil-sparing third nerve dysfunction.[130] Previous compromise of the third nerve by tumor influences a patient’s prognosis. None of the 19 patients who had preoperative third nerve palsies experienced complete recovery or substantial improvement. Since one of the indications for intervention was a patient’s desire to eliminate diplopia, evidence of third nerve dysfunction was a very poor prognostic marker of complete recovery following cavernous sinus surgery.

Our data support the initial observation of Dolenc and colleagues,[98] who noted that although there was a substantial incidence of third nerve palsies postoperatively, most cleared. One hundred four (90.4%) of 115 patients with intracavernous aneurysms who had undergone surgery developed third nerve palsies; all but 7 (6.1%) recovered.[131] All of our patients with incomplete third nerve palsies postoperatively (and without evidence of third nerve dysfunction preoperatively) recovered completely. On the other hand, there are long-term follow-up data on 30 of the 40 patients who had complete postoperative third nerve palsies and only 8 cases (27%) cleared completely. Another 4 patients (13%) failed to recover at all (all of whom had partial involvement preoperatively) (Figure 6), and of the remaining 18 (60%) who had partial recovery, 9 (50%) developed aberrant regeneration (Figure 5).

TRIGEMINAL DYSFUNCTION

Although some of the neurosurgical literature mentions “dry eye,” little emphasis has been given to developing severe corneal problems in anesthetic corneas. Recovery of impaired trigeminal function occurred less often than recovery of ocular motor function. Those patients who had a persistently anesthetic cornea were at risk for developing neurotrophic keratitis. Of the 28 patients with long-term follow-up, neurotrophic keratitis developed in 12 (43%). Additional risk factors for the development of keratitis included compromise of facial nerve function and aqueous tear deficiency. There is not enough data to analyze the effect of sectioning the

greater superficial petrosal nerve and its loss of parasympathetic innervation to the lacrimal gland. Patients with recognized corneal anesthesia must be treated aggressively and followed up very carefully.

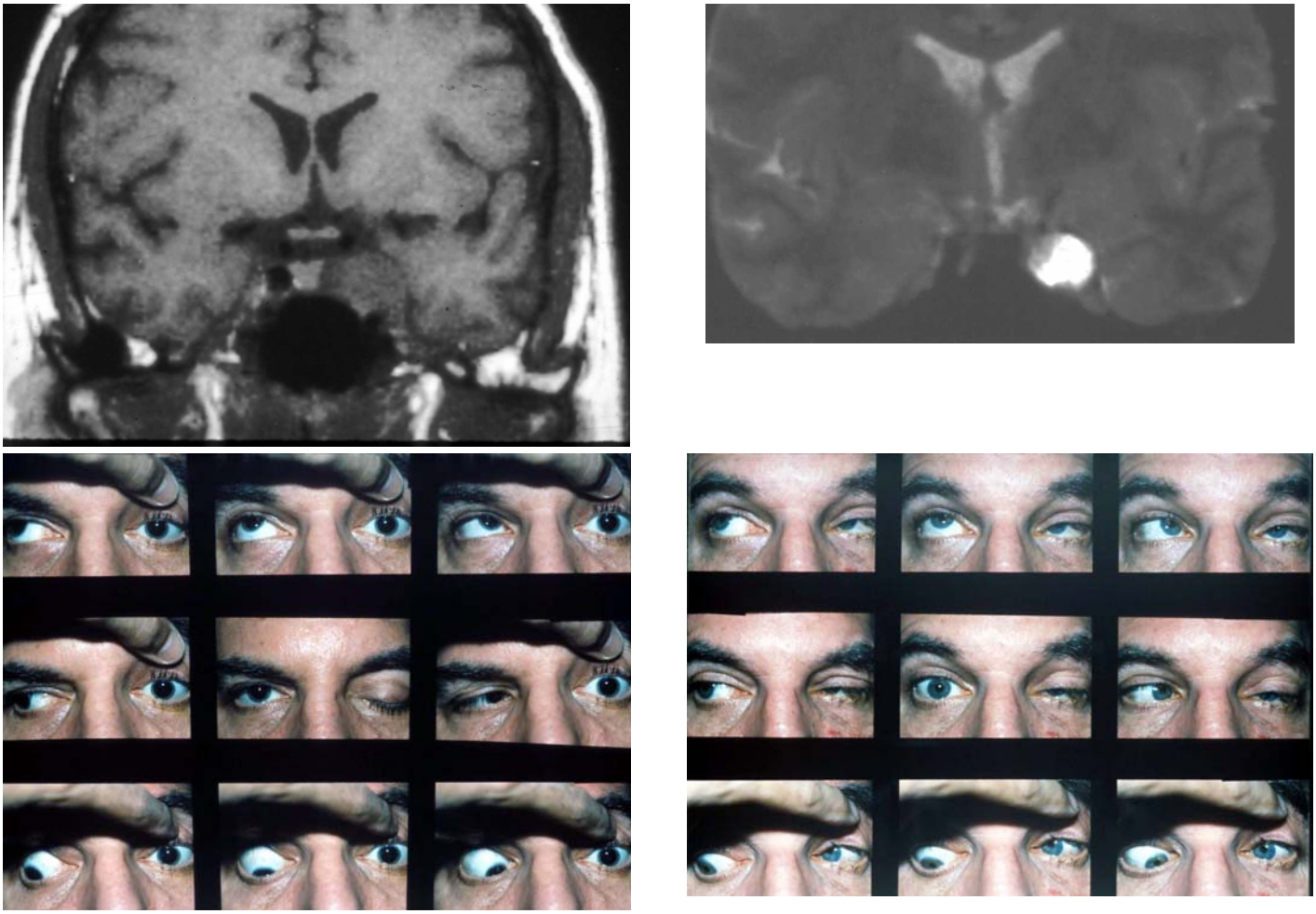

FIGURE 6

Case 17. A 52-year-old patient was referred to the neuro-ophthalmology unit in June 1990 with a 3-year history of double vision and headache. He had undergone exploration of the middle cranial fossa in February 1987, but no biopsy was taken. MRI revealed a mass in the left cavernous sinus dark on T1 (top left) and bright on T2 (top right). On examination, his afferent system was entirely normal, with 20/15 and 20/20 visual acuity. Fields were also full and motility was unremarkable, with no evidence of ophthalmoplegia. On June 19, 1990, he underwent a left pterional craniotomy with resection of a meningioma involving the cavernous sinus. Postoperatively, acuity remained normal, with no afferent pupillary defect and normal fields, but he developed a complete left ophthalmoplegia and loss of corneal sensation (bottom left). His postoperative course was complicated by a cerebrospinal fluid leak. The residual tumor around the carotid artery was subsequently treated with gamma knife. Follow-up at 2 months and 14 months showed minimal recovery of lid function but essentially complete persistent ophthalmoplegia and continued loss of sensation OS (bottom right). He had 45 diopters of esotropia in primary position. Two patients who were completely normal preoperatively developed complete persistent ophthalmoplegia postoperatively. Long duration and possible previous surgery may have predisposed this patient to these complications, but the exact mechanism remains obscure.

OPHTHALMIC REHABILITATION

Treatment of patients with cranial nerve palsies induced by cavernous sinus surgery depends on the functionality of the cranial nerves themselves. Few options exist to improve optic nerve function, although patients with significant optic neuropathies following cavernous sinus surgery may benefit from low-vision aids available to other patients with persistent optic nerve dysfunction. Patients with trigeminal dysfunction are best treated with aggressive lubrication. It is imperative to ensure adequate lid closure, and the presence of a seventh nerve dysfunction in the setting of corneal anesthesia is a disaster waiting to happen. Lid retraction may be treated surgically to promote corneal protection, and lower lid retraction may respond to placement of a hard palate graft (Figure 5).

One must also recognize other risk factors, including dry eye and a limitation in vertical movement. Punctal plugs may decrease tear outflow. The use of high-viscosity lubricants may be more effective but can also blur vision. Finally, in patients with persistent epithelial breakdown, vascularization procedures to the cornea may prevent perforation and loss of the globe. The simplest, a Gunderson flap (recommended in 1 patient with persistent epithelial defect), brings the conjunctival vessels over the cornea.

Following cavernous sinus surgery, diplopia may not be an immediate concern because the eyelid is often ptotic due to either a third nerve palsy or swelling associated with the craniotomy. As the swelling resolves and lid function recovers, patients may complain of double vision. In the short term, the simplest way of dealing with this is by occlusion. At least initially, the deviation is usually incomitant enough not to respond to the use of prisms, although in highly motivated patients, an area of binocularity can be established or the eccentric area of binocularity can be moved to primary position. Fresnel stick-on prisms are the least expensive solution and permit treatment of larger deviations than ground-in prisms. Unfortunately, Fresnel prisms will blur vision. Botulinum toxin injections have been used in patients with cranial nerve dysfunction. There is no question that injections into the medial rectus in a patient with a complete sixth nerve palsy may delay development of medial rectus contracture and progressive esodeviation of the affected globe. It is unlikely, however, that botulinum toxin injections will result in functional binocularity in patients and probably should not be offered on that basis. There is also a reasonable incidence of recurrent ptosis associated with botulinum toxin injections due to leakage of the botulinum toxin as well as the potential for inducement of vertical movement problems on top of the already existing cranial nerve palsies.

From a functional point of view, the fourth nerve is certainly the easiest to deal with, and new involvement is probably the least concern. If this is isolated and stable, an ipsilateral inferior oblique weakening procedure or, alternatively, a contralateral inferior rectus weakening procedure should result in alignment.

The difference between complete and incomplete sixth nerve palsies is substantial from a functional point of view. Although it is possible to significantly increase the area of binocularity in patients with incomplete sixth nerve dysfunction with relatively simple, horizontal recession and resection procedures, those patients with complete sixth nerve dysfunction have a much poorer prognosis for complete resolution of diplopia. It is possible to align even these patients with transposition procedures, but the area of binocular single vision is usually significantly limited (Figure 5).

Although less commonly seen as an initial manifestation of cavernous sinus pathology, postoperative third nerve dysfunction may be the greatest challenge to ocular rehabilitation. Although one can argue that realignment of a patient with complete sixth nerve palsy is not trivial, this pales in comparison with an attempt to regain functional binocularity in a patient with a complete or even incomplete but severely compromised third nerve.

Surgical intervention for realignment should always be delayed until full recovery has occurred. Early cranial nerve dysfunction in our patients often cleared within a period of weeks to 1 or 2 months, but late improvement was also possible. Quantitative assessment of ocular motility with the use of Hess screen and binocular single vision field testing is probably the best means of assuring stability before consideration of muscle surgery. In patients with persistent cranial nerve dysfunction, often there is substantial residual limitation of globe duction. This is particularly true in patients who develop aberrant regeneration. Although it is possible to move the area of binocularity with muscle surgery on that eye, an increase in the binocular single vision requires procedures that limit rotation of the opposite eye. The Faden posterior fixation operation has been particularly useful in expanding areas of binocularity as well as moving them to more functional locations. By limiting the excursion of the normal eye, more extensive binocularity may be achieved (Figure 7).

CLINICAL CONSIDERATIONS AND HISTORICAL DISCUSSION

Can the Surgery Be Performed?

The prior warnings against surgery within the cavernous sinus were predicated on what was believed to be the unavoidable severe risks. As published in 1906, Frazier[30] described removing a tumor from the area of Meckel's cave but the threat of bleeding kept most surgeons out of this extradural region. In the early 1960s Dwight Parkinson[57] became interested in the anatomy of the cavernous sinus. These studies formed the basis of his first operation on a vascular lesion within the cavernous sinus, which he reported in 1965.[1] He adapted the use of hypothermia and circulatory arrest, previously used in the treatment of intracranial aneurysms,[132] to reduce intraoperative bleeding. Based on this case and subsequent experience, in 1982 Parkinson and West[133] wrote, "an operative approach to this space is indicated when it is anticipated the lesion can be removed." In this statement he clearly defined the goals of surgery to include complete excision of the pathology present. In the case of a vascular abnormality, such as an aneurysm or carotid cavernous fistula, it is easy to monitor the completeness of a resection, but determining total removal is much more difficult with neoplasia. Malignant tumors in particular have an extremely high incidence of recurrence, and these tumors often reappear despite aggressive en bloc resection.[134] Because of the difficulty in completely excising malignant tumors, Parkinson and West[133] suggested that "malignant tumors arising from the nasopharynx, metastases, and chordomas should not be approached in this space since the entire lesion cannot be removed." Other investigators assert that quality of life can be improved with a surgical approach,[135] even if complete excision is not possible and recurrence is inevitable. This series and others suggest that technically surgery within the confines of the cavernous sinus is possible with a relatively low mortality.

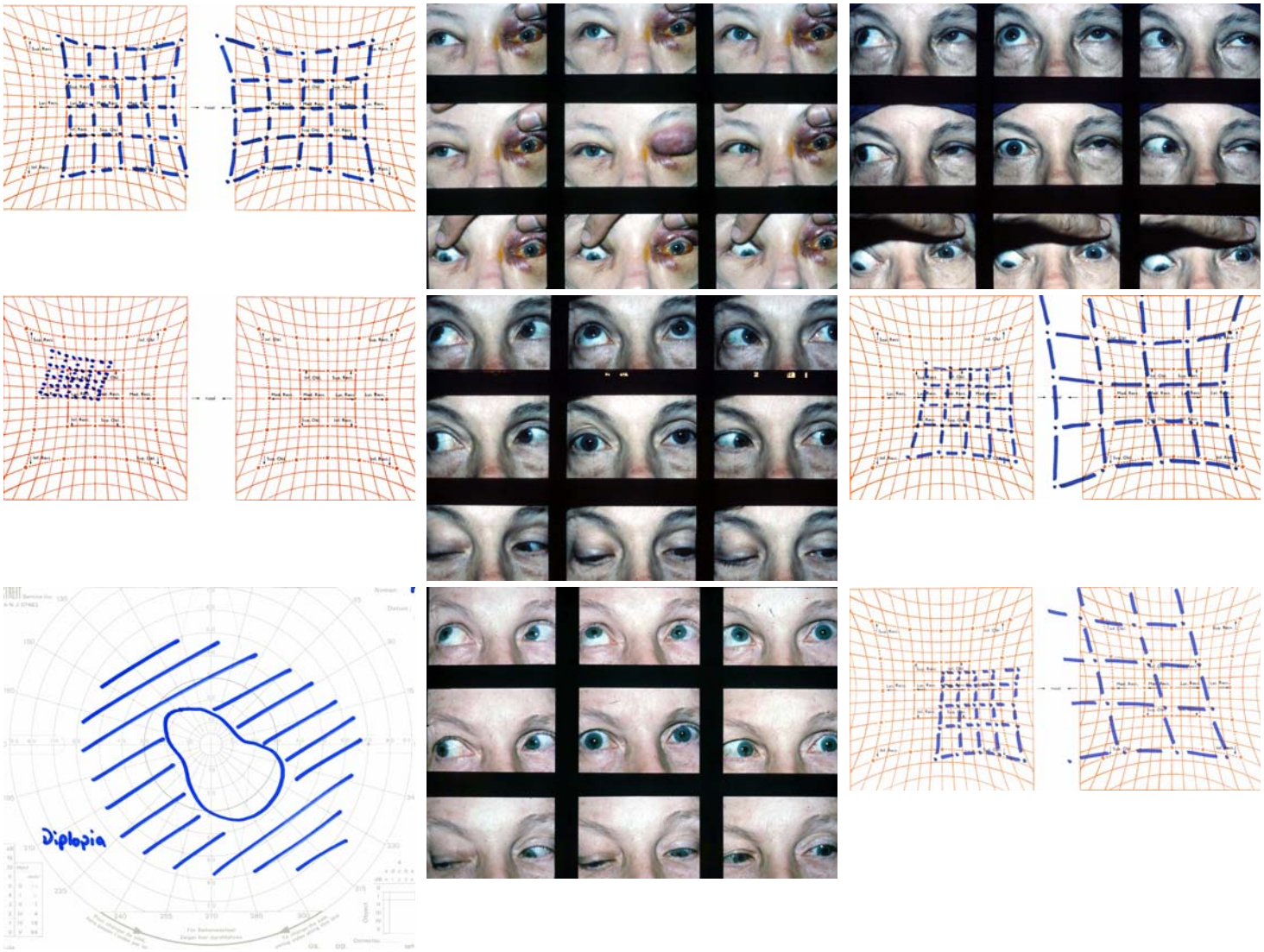

FIGURE 7

Case 22. A 57-year-old right-handed patient was referred on January 29, 1991. At that time, she gave a history of 10 months of horizontal diplopia. When the double vision failed to clear, an MRI scan demonstrated a left-sided parasellar meningioma, and she underwent a craniotomy and subtotal resection. The operation was terminated when it was realized that the meningioma encased the carotid and extended into the cavernous sinus. On examination, her visual acuity was 20/20 and 3pt OU. There was no evidence of afferent pupillary defect. She had an esodeviation increasing on left gaze and a left hyper increasing on right gaze and with left head tilt (row1 left). She was felt to have a left sixth and left fourth nerve palsy. On January 31, 1991, she underwent a frontotemporal craniotomy with resection of a meningioma extending into the left cavernous sinus. The left carotid artery ruptured during the procedure and was occluded. Her perioperative course was further complicated by a cerebrospinal fluid leak. Postoperatively, she had complete ophthalmoplegia OS, with a nonreactive pupil (row 1 middle). In addition, she was noted to have a left afferent pupillary defect. Three months after surgery, the left lid began to elevate, associated with some recovery of elevation, depression, and adduction. She still had a partial left third nerve palsy and absent corneal sensation (row 1 right and row 2 left). One year after surgery, visual acuity had improved to 20/25 OS, but she still had a .9 log unit left afferent pupillary defect. Visual fields demonstrated a persistent arcuate visual field defect OS. Her motility examination revealed mild to moderate limitation in abduction, moderate limitation in elevation, and moderate limitation in vertical movements, with lid elevation suggestive of aberrant regeneration (row 2 middle and right). She also had evidence of mild neurotrophic keratitis, with inferior corneal rose bengal staining. Binocular single vision fields demonstrated single vision with a slight gaze to the left, but otherwise there was relatively good fusion (row 3 left). She had diplopia with right gaze. She was seen periodically in follow-up with a slight change in head positioning until July 1998, when she complained of increasing head turn. At that time, visual acuity was 20/25 OU, with a 1.2 log unit left afferent pupillary defect. She had marked limitation in elevation OS and moderate limitation of abduction (row 3 middle and right) felt to indicate residual incomplete sixth and third nerve palsies. (continued)

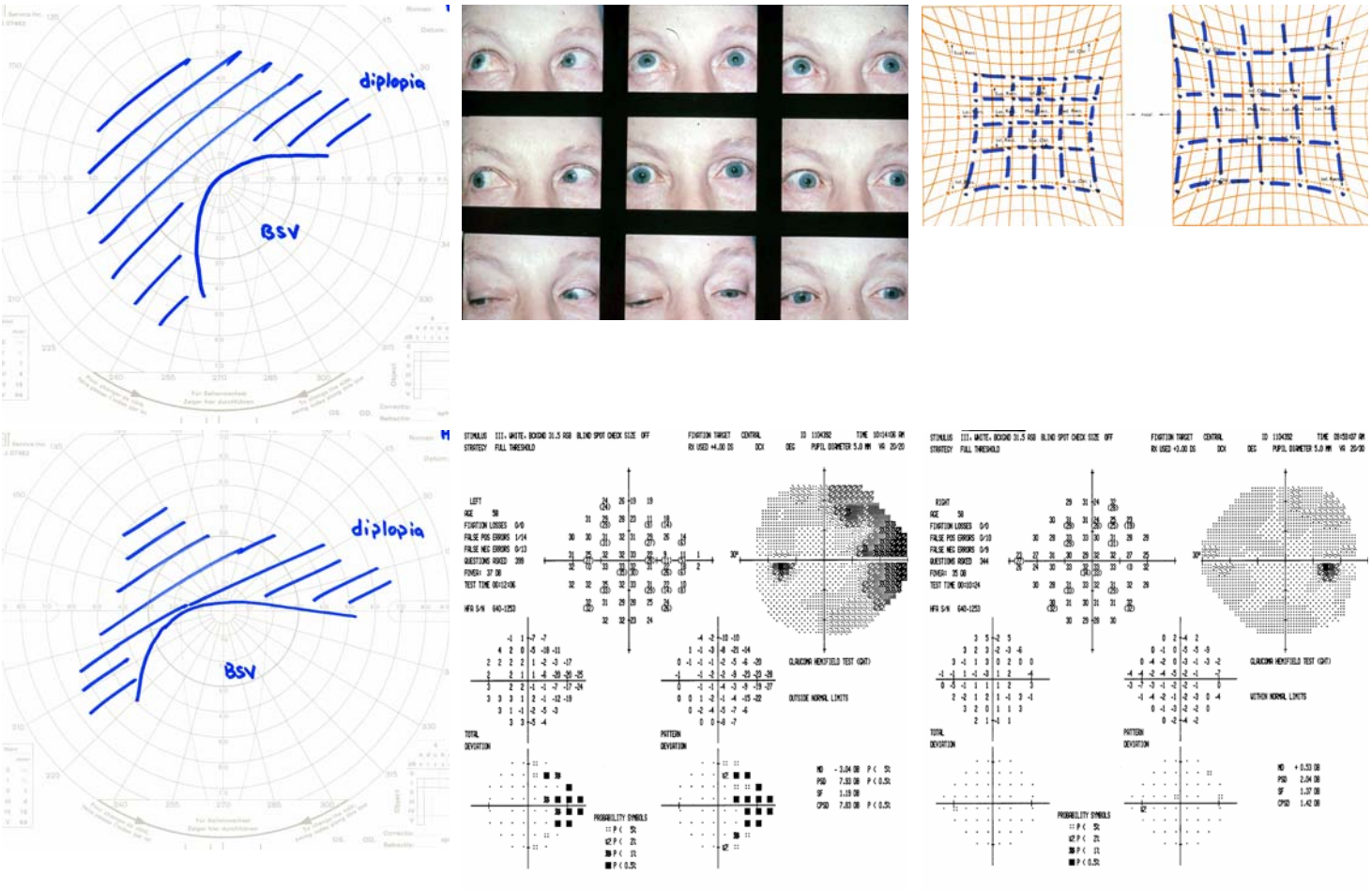

FIGURE 7 (contintued)

She measured 25 diopters of left esotropia in primary position. Her binocular single vision fields demonstrated the shift of the binocular field to the right side, with diplopia to the left (top left). On August 10, 1998, she underwent a right 6-mm medial rectus recession and Faden procedure. One month postoperatively her motility had improved (top middle). The area of binocularity shifted substantially to the left side, as demonstrated by Hess screen (top right) and binocular single vision field (bottom left). Clinically she had a reduction in her head turn and symptomatic improvement in her diplopia. Although she was unaware of any problems with her vision, her visual fields continued to demonstrate arcuate visual field defects in the left eye (bottom middle) and a normal field on the right (bottom right). This patient demonstrates many of the potential problems in cavernous sinus surgery. Her carotid artery was encased by the meningioma, and during surgery it ruptured. Although she did not have evidence of a cerebral infarct, she did show signs of a new left optic neuropathy, even though she recovered good central acuity. With her normal central vision, it is likely that her optic nerve compromise would have gone undetected on less than a detailed examination. She had complete postoperative ophthalmoplegia with partial clearing of both her third and sixth cranial nerve palsies, but with development of aberrant regeneration of her oculomotor nerve. Initially, she could fuse centrally, but with time, she developed an increasing head turn. As the motility OS could not be improved, the best way of achieving an increase in binocularity was to partially paralyze the right eye. A Faden procedure, by limiting adduction OD, substantially increased her area of binocularity.

Can the Tumor Be Removed?

The seemingly simpler question is whether we can completely remove "benign lesions" from the area of the cavernous sinus. In the aforementioned discussion, Parkinson and West went on to suggest a "preoperative diagnosis of either an aneurysm, a meningioma, or neurofibroma would justify this belief." Unfortunately, the ability to completely remove even benign tumors within the area of the cavernous sinus may not be as easy as it seems. This is particularly true of meningiomas for which intimate relationships to the surrounding carotid artery and nervous structures often make complete resection impossible. Although DeMonte and coworkers[136] reported complete excision in 31 (76%) of 41 patients, investigators in earlier series reported much lower percentages. Lesoin and colleagues[137] were able to resect meningiomas completely in only 3 (14%) of 21 cases. Even some of the more recent series demonstrate lower percentages. Kim and associates[138] reported complete resection of only 10 (48%) of 21 meningiomas, and Knosp

and colleagues[139] achieved only a 17% complete resection rate. In a recent series O'Sullivan, and coworkers[140] reported complete resections in 26%. Involvement of the lateral aspect of the cavernous sinus may permit a higher rate of complete excision.[141]

Recurrence can happen even with complete excision, and a 10% to 25% incidence has been reported.[136,138,140,142] The rate of recurrence seems to increase with the duration of follow-up, and previous studies of meningiomas in general suggest that the longer the follow-up, the greater the recurrence rate. Mirimanoff and colleagues[143] reported recurrence rates for all meningiomas as 7%, 20%, and 32% at 5, 10, and 15 years of follow-up, respectively. Cavernous sinus numbers are likely to be higher.

The extremely slow growth and variable nature of these tumors are major factors in making it difficult to determine recurrence rates. Another cause for frequent recurrence is the invasion of the vascular wall[98,144,145] and the involvement of the cranial nerves themselves.[146] As seen in our cases, carotid and cranial nerve invasion occurs even with benign tumors and limits possible complete resection.

Progression rates are clearly higher if tumor is intentionally left along the carotid and around the cranial nerves. In reviewing a series of 225 subtotally resected meningiomas in all locations, Mirimanoff and colleagues[143] found progression in 37% at 5 years, 55% at 10 years, and 91% at 15 years following surgery. Mathiesen and associates[147] found that 42 (61%) of 69 patients (out of a series of 315 skull base meningiomas operated on between 1947 and 1982) who were treated with subtotal resection died of disease usually by 10 years. There is less data (and of shorter duration) on incompletely resected cavernous sinus meningiomas, but after 2 years of follow-up, O'Sullivan, and associates[140] reported 2 (6.5%) of 31 cases with progression, and De Jesus and colleagues[148] detected 7 (15%) of 46 patients who showed progression (mean follow-up, 34 months). The frequency of progression was up to 38% in those patients who had been followed for more than 5 years. Earlier studies also found that the extent of the original excision was the best prognostic factor determining recurrence.[149] These data support an argument for more aggressive attempts at complete excision, but the recurrence rates clearly indicate that even with total surgical resection, meningiomas may recur. Unfortunately, more aggressive surgery probably carries a higher risk of morbidity.[150]

Recent advances in molecular genetics reveal chromosomal changes[151-153] that put patients at high risk for recurrence and progression. There is hope that these and other molecular genetic markers may indicate the risk of recurrence in the future.

In our series the acknowledged residual tumor and the high incidence of subsequent gamma knife treatment underscore the difficulty in achieving complete resection of lesions involving the cavernous sinus. It is often difficult, if not impossible, to make definitive statements about complete excision without more detailed long-term follow-up. The slow growth of many of these lesions continues to be a challenge to surgery in the parasellar region.

Are the Results Different for Nonmeningiomatous Benign Tumors?

Theoretically, patients with nonmeningiomatous benign tumors involving the cavernous sinus should have better prognoses. Day and Fukushima[154] reported complete clinical resection in 29 (76%) of 38 trigeminal neurilemomas. Sekhar and colleagues[155] published a series on complete clinical resection in 30 (79%) of 38 patients with benign nonmeningiomatous tumors involving the cavernous sinus. These tumors included neurilemomas, pituitary tumors, cavernomas, craniopharyngiomas, epidermoids, and juvenile angiofibromas. Eisenberg and associates[156] reported similar statistics in a mixed series of nonmeningiomatous tumors affecting the cavernous sinus, with complete clinical resection in 33 (82.5%) of 40 patients.

Unfortunately, recurrences are still possible even in completely resected nonmeningiomatous tumors. This is particularly true of invasive pituitary tumors in which complete surgical excision may not be possible. Eisenberg and colleagues[156] reported a 28% incidence of recurrence. Based on the results of transphenoidal surgery series for pituitary marcoadenomas, it is likely that longer-term follow-up will reveal even higher rates of recurrence.

Dolenc[111] noted one of 40 trigeminal neurilemomas recurring in 1994, and Taha and associates[157] found a 10% incidence of recurrence of trigeminal neurilemomas. Sekhar and coworkers[158] reported 4 (13.3%) of 30 nonmeningiomatous benign lesions recurring within the area of the cavernous sinus.

All of these numbers are substantially better than the statistics from series published before the development of skull base approaches. Recurrence rates of up to 65% have been reported in patients previously treated. This likely reflects not only the improvements in surgical approaches, but also the ability to better define the anatomy with the advent of neuroimaging studies. Although the numbers are an improvement, recurrence is still possible, even with reported complete clinical excision.

Unfortunately, the effect of the nature of the pathology on the incidence of neuro-ophthalmic complications has not been previously addressed. Somewhat surprisingly in this study, when the data was subject to rigorous quantitative assessment, there was little difference between the complication rates for patients that were found to have meningiomas and those with nonmeningiomatous pathology. This was particularly true for the chance of optic nerve damage. Nonmeningiomas did have a better chance of complete recovery of pre-existing cranial nerve palsies, although the incidence was low.

Can We Improve Patient Symptoms?

The goal in operating on lesions within the cavernous sinus (other than complete cure of the tumor) is to improve the patient's symptoms. Cavernous sinus lesions may enlarge to secondarily involve the optic nerve even though it is not within the sinus proper. Improvement in compromised optic nerve function can be expected with optic nerve and canal decompression during cavernous sinus surgery. Five (15%) of 33 patients showed improvement in optic nerve function in the series reported on by DeMonte and colleagues.[136] Kim and associates[138] found improvement in optic nerve function in 1 of 7 patients. In the present series, improvement occurred in 5 (25%) of 20 patients.

Unfortunately, but not surprisingly, no patient with complete optic neuropathy improved following surgical decompression in the

area of the cavernous sinus.[98] This has also been demonstrated in the present study; none of the 4 patients with hand motion vision or worse, including 1 meningioma, experienced improvement. On the other hand, one could argue that decompression of the optic nerve might be accomplished without invading the cavernous sinus, inviting the attendant morbidity described.[159]

Given that the majority of patients with cavernous sinus pathology present with evidence of ocular motor abnormalities, one of the hoped-for results of cavernous sinus surgery is an improvement in ocular motility. Early reports were encouraging. Lesoin and associates[137] reported improvement in ocular motor function in 10 (48%) of 21 patients. Sekhar and colleagues[158] reported improvement in 7 of 9 patients with third nerve palsies, 2 of 6 patients with fourth nerve palsies, and 6 (50%) of 12 patients with sixth nerve palsies in a series of mixed pathology. Somewhat more ominous was the report in 1991[120] that while 24 (44%) of 54 patients showed improvement in ocular motor function following cavernous sinus surgery, none of the 18 patients with meningiomas improved.

This poorer prognosis in meningiomas has been confirmed in subsequent reports. In a series restricted to meningiomas, DeMonte and associates[136] found improvement in ocular motor function in only 13%, whereas patients with nonmeningiomatous tumors reportedly had a 50% improvement.[156] In all patients, the third nerve was much less likely to recover than the sixth nerve.[156] The ability to improve preexisting ocular palsies was very limited in the present series. In only 1 patient was there felt to be improvement in a preexistent third nerve palsy (none cleared completely), and only 2 patients with sixth nerve palsies improved (clearing in one).

How Do We Assess Cranial Nerve Function?

Throughout these published series there are few data to indicate how cranial nerve function was assessed. Biglan and associates[160] established a clinical grading system of binocularity in an attempt to improve clinical relevance. In this system, binocularity is graded as "excellent" if the patient has no diplopia in the primary position and downward reading gaze, and at least 20 degrees to either side. Binocularity is classified as "good" if there is no diplopia in the primary and reading gaze but double vision with any eccentric gaze. Patients were recorded as having a "fair" condition if elimination of diplopia required a head turn and a "poor" condition if there was diplopia in all fields of gaze.

This classification system was used by Cusimano and colleagues[142] to follow 124 patients who underwent cavernous sinus surgery. Four (27%) of the 15 who had poor preoperative binocularity improved to "good" or "excellent" status, and 6 (20%) of 30 patients with "good" preoperative binocularity improved to "excellent" status. The series included meningiomas and nonmeningiomatous tumors. Even in this series, there was little quantitative assessment.

The potential of completely excising a lesion and improving function must be balanced against the surgical potential for creating new problems as well as the natural history of the lesions themselves. The variability in the natural history of cavernous sinus tumors is a major limitation. In particular, menigiomas involving the cavernous sinus often have an extremely indolent history, exhibiting very slow progression. One of the difficulties in analyzing previous series that focus on the natural history is the variable inclusion criteria. The natural history is far worse if tumors arising from the clivus or petrous bone and secondarily involve the cavernous sinus are included, because these tumors will often compress the brainstem. If the series are restricted to tumors involving the cavernous sinus in isolation, the natural history is far more benign.

What Is the Natural History of Lesions Affecting the Cavernous Sinus?

There are few series that provide natural history data. In a series of 8 patients followed up for a mean of 5.5 years, Freidlander and colleagues[161] reported progression in only 1 patient. In a series of 24 patients observed at Johns Hopkins for a mean of 76 months, there was evidence of clinical progression in only 6 (25%).[162] In an updated follow-up of 29 patients with at least 10 years of study Klink and associates[72] found new motility defects in only 3 (10%) but noted new optic nerve dysfunction in 7 (24%). We sometimes forget that the clinical findings are more important to the patient than are minute measurable changes on imaging studies. Patients are more concerned about worsening double vision or a decrease in acuity than radiographic changes. When dealing with the long-term natural history of a tumor, it is important to consider the clinical symptoms as paramount. This slow growth makes even most recent series of surgical results difficult to interpret as the mean follow-up is usually 5 years or less.[147]

What Is the Expected Morbidity of Cavernous Sinus Surgery?

Can we operate safely within the cavernous sinus without inducing significant morbidity? Since the beginning of the modern era of skull base surgery, surgical mortality has been substantially reduced. Dolenc and coworkers[98] reported 4 deaths (6.3%) out of 63 patients who had undergone cavernous sinus surgery. More recent series have reported the incidence of death in 2 (3.7%) of 54,[120] 3 (7.3%) of 41,[136] and 2 (9.5%) of 21 postsurgical patients.[138] In the present series, 2 patients died within the perioperative period (2.4%), only 1 with a meningioma (1.75%).

Lesser complications have been far more frequent and have included infarction with hemiparesis,[136,138,142] meningitis, and hydrocephalus. A CSF leak is one of the most frequently occurring complications following cavernous sinus surgery and is probably a direct result of surgical aggressiveness. Its incidence may be as high as 28%.[142]

A sobering statement was made in Cusimano's 1995 summary of the Pittsburgh[142] experience: "the majority of patients in this series suffered a surgical complication." Although he goes on to point out that most complications were minor or treatable, this potential must be weighed against the expected benefits of surgery. For psychological and other reasons, a case can still be made for aggressive surgery.[163]

It is not the role of the ophthalmologist to discuss nonophthalmic risks with the patient without including the referring surgeon. Unfortunately, there is often a tendency for neurosurgeons to trivialize the morbidity in any transcranial procedure. As

ophthalmologists are often the ones to recognize cavernous sinus pathology and thus refer patients to neurosurgery, it is useful to have a feel for the interaction of the neurosurgeon with the patient so that all parties are aware of the goals as well as the risks of any type of intervention.

What Are the Problems of Nonquantitative Ophthalmic Testing?

The major potential for complications in cavernous sinus surgery involves damage to those cranial nerves contained in the cavernous sinus. Given that these nerves have a profound effect on ophthalmic function, it is surprising that ophthalmologists have provided little direct input into assessing these patients both preoperatively and postoperatively.[72,160,162] The lack of detailed quantitative ophthalmic testing is illustrated by the way some of the cranial nerve deficits are reported. In Hakuba and colleagues'1989 report of 10 intracavernous tumors, [26] they state that "a transient paresis of the third to sixth cranial nerves was seen in five patients." Unfortunately, the report does not identify which nerves, the severity of the paresis, and exactly how these were measured. In addition, the enthusiasm for the results of surgery may explain why 9 of the 10 patients were said to have "excellent or good" results, despite the fact that 5 patients were noted to have permanent, complete ophthalmoplegia. Defining "good" and "excellent" is not so obvious in many of the previously reported series. Another question here concerns how well these patients were truly evaluated. In Al-Mefty and Smith's 1988 series,[164] 18 patients were reported on following cavernous sinus surgery. The first 13 patients underwent surgery in Saudi Arabia, and the last 5 patients underwent surgery at the University of Mississippi. Of the 18 patients, only 4 were noted to have cranial nerve palsies, with a third nerve palsy in 3, a fourth nerve palsy in 1, and a fifth nerve palsy in 1. If the details of the series are reviewed, one finds that all 4 of the patients with cranial nerve palsies were operated on at the University of Mississippi (of 5 patients), whereas no patient (of 13 patients) who was operated on in Saudi Arabia (an earlier part of the series) was noted to have a cranial nerve palsy. One has to be suspicious that the earlier patients were not evaluated in as much detail as the subsequent patients.

As mentioned in our oculomotor results, none of the neurosurgical series discusses the concept of aberrant regeneration. The only time this is brought up is in those reports detailing intraoperative cranial nerve repair.[165-167] This is somewhat surprising given that meningiomas in the parasellar area may be responsible for the development of aberrant regeneration in the absence of a history of a third nerve palsy.[168] The combination of the classical findings of aberrant regeneration without a history of a third nerve palsy (primary aberrant regeneration) is almost pathognomonic of a meningioma or aneurysm in the parasellar region.

What Are the Particular Problems Associated With Ocular Motor Nerve Dysfunction?

Even at the outset of the modern era in skull base surgery, concerns were expressed about the potential for damage to the third nerve. Lesoin and colleagues[137] stated that it was "not possible to completely remove an intracavernous meningioma without disturbing the ocular motor nerves." Despite these concerns, initial reports seemed to be encouraging. Only 5 (24%) of 21 cases[137] demonstrated worsening of third nerve function postoperatively. Perneczky and colleagues[122] reported 2 cases (5.7%) of third nerve palsy in 35 patients who had undergone surgery in which a subtemporal lateral approach was used. Of 42 original patients reported on (from Pittsburgh), 10 (23.8%) had a "temporary" palsy, but none had permanent third nerve dysfunction. By 1991 Sehkar and associates[169] recognized 6 (5.9%) of 101 patients with permanent third nerve dysfunction. Al-Mefty reported transient third nerve palsies in 3 (4.1%) of 74 cases and permanent third nerve dysfunction in 3 others (4.1%) (in 7 patients [9.5%] it was "too early to tell.").[99] DeMonte and colleagues[136] found 2 (14.3%) of 14 patients with preoperative third nerve palsies to have worse dysfunction and 2 (14.3%) of 14 patients without preoperative third nerve palsies to have developed new ones. Even with nonmeningiomatous tumors, third nerve palsies may develop or worsen. Eisenberg, and associates[156] reported 4 (12.5%) new third nerve palsies among 32 patients who had undergone surgery and worsening palsy in 1 (12.5%) of 8.

Because of the innervation of multiple muscles, damage to the third cranial nerve often results in incomplete resolution, with evidence of variable muscle misfiring. Not until the first third of the 20th century did explanations for this misdirection syndrome appear in the literature.[170] Morris Bender, a neurologist in New York, undertook experimental work with oculomotor nerve regeneration in which he sectioned the third nerve of a chimpanzee and followed its recovery.[171] Walsh[172] reviewed the importance of aberrant regeneration in 1947. It has been suggested that there may be alternative explanations for aberrant regeneration, including ephaptic transmission,[173] but it is likely that actual reinnervation of sprouting axons terminating in the wrong extraocular muscles is responsible for the majority of the findings. The classic finding of lid elevation with attempted depression and adduction is probably less consequential than the coinnervation of the superior and inferior rectus muscles, which leads to persistent limitation in the vertical gaze. Aberrant regeneration is probably underdiagnosed and is the responsible mechanism in the majority of patients with incomplete third nerve palsies and vertical compromise.

It is unlikely that the attempts at surgical repair of the third nerve during cavernous sinus surgery will reduce the incidence of aberrant regeneration. At this time, the best treatment for aberrant regeneration is to prevent its occurrence. Aberrant regeneration does not occur with presumed microvascular third nerve palsies, and its high incidence in patients undergoing cavernous sinus surgery suggests that perhaps there is more than simple vascular damage to the third nerve. It is possible that retained tumor within the nerve or direct surgical trauma results in misdirection in patients following cavernous sinus surgery. The possible development of aberrant regeneration has been one of the strongest arguments in favor of limiting surgery.[72,161]

The current series has a much higher incidence of third nerve dysfunction. Only 1 (1.8%) of 57 patients showed no evidence of third nerve dysfunction immediately postoperatively. Exclusion of the 19 patients with preoperative third nerve dysfunction still results in a 97% incidence of acquired third nerve palsy immediately following cavernous sinus surgery. Although most palsies cleared rapidly, 4 (11%) of the 35 patients with long-term follow-up had complete third nerve dysfunction, and an additional 18 (51%) had an incomplete third. Nine (26%) demonstrated evidence of aberrant regeneration. Probably the closest numbers to the current

series were reported by Cusimano and colleagues,[142] who noted that 35 (60%) of 58 patients undergoing cavernous sinus surgery had binocularity that was "worse than excellent."

Sindou and Pelissou,[174] in a literature review, reported on new fourth nerve palsies in 4 (7.3%) of 55 patients undergoing surgery for trigeminal neurilemomas. In Al-Mefty and Smith's original report of 18 patients,[164] only 1 (5.6%) had a fourth nerve palsy. Nine (12.2%) of 74 patients in their expanded series[99] were said to have fourth nerve dysfunction (although the situation in 7 patients was listed as "too early to tell."). Perneczky and colleagues[122] found 2 (5.7%) fourth nerve palsies among 35 cases. The Pittsburgh group originally reported 9 (20.9%) temporary and 4 (9.3%) permanent fourth nerve palsies in 43 patients.[158] The incidence had changed to 7 (7.7%) of 91 cases[165] by 1991, and in an article later that same year, 11 (10.9%) of 101 cases.[169] In more recent series, new fourth nerve palsies occurred in only 1 (3.7%) of 27 patients undergoing cavernous sinus surgery.[136] Although the fourth nerve is theoretically at greater risk during surgery for meningiomas than nonmeningiomatous tumors within the cavernous sinus, Eisenburg and associates[156] reported 4 (11.1%) of 36 patients with new fourth nerve dysfunction.

In the current series, fourth nerve palsies could not be separated from other cranial nerve palsies. When the third and sixth nerve palsies were complete, the fourth nerve usually showed no function.

The sixth nerve is the most difficult to see during surgery because it is situated deep within the cavernous sinus, in relation to the carotid artery. Early cavernous sinus surgical series report worsening sixth nerve function in patients in whom it already existed. In the original series of cases from Pittsburgh, there were 12 preoperative abducens palsies and 14 temporary palsies postoperatively. In only 4 (9.5%) of the 42 cases was sixth nerve dysfunction said to be permanent.[158] When the series was updated to include 101 patients,[169] there were 10 permanent palsies (10%). Interestingly, a report earlier that year had revealed only 5 sixth nerve palsies (5.5%) among 91 patients undergoing surgery.[166] This difference raises the question of how closely the patients were monitored for evidence of sixth nerve dysfunction. Five (9.3%) of 54 cases in the series from Hanover had permanent sixth nerve dysfunction, and 10 had temporary abduction abnormalities.[120] Only one (1.4%) of 74 cases reported in 1991[99] was said to have a permanent sixth nerve palsy, although 7 were listed as "too early to tell." Two (11%) of 18 patients with sixth nerve dysfunction preoperatively were reported to be worse following surgery.[136] When broken down into nonmeningiomatous benign tumors, there were still a number of new sixth nerve palsies following surgery (4 [14.3%] of 28 reported by Eisenberg[156]).

There was no indication of the means used to assess cranial nerve function in any of these reports. None of these previously reported series include the numbers of patients with cranial nerve dysfunction seen in this current series. Only 8 patients (10%) had no evidence of sixth nerve dysfunction immediately after surgery. Although many of these dysfunctions resolved, 35 (69%) of 51 patients had some evidence of sixth nerve dysfunction at the follow-up more than 3 months after surgery, and 14 (27%) had a complete sixth nerve palsy.

Although there may be several explanations for the higher incidence of cranial nerve palsies in our postoperative patients, it is likely that quantitative detailed assessment may be largely responsible for explaining the higher numbers. Incomplete ophthalmoplegia is not incompatible with binocularity and good visual function, but may well lead to significant patient dissatisfaction. Future studies will need to include methods to evaluate functional outcome.

What Are the Implications of Trigeminal Dysfunction?

The clinical importance of the fifth cranial nerve is seldom emphasized, although it is among the cranial nerves which may be injured during cavernous sinus surgery. The true implications of neurotrophic keratitis as a potential complication of cavernous sinus surgery have largely been ignored, although dry eye and its potential connection to the greater superficial petrosal nerve (responsible for reflex tearing) have been discussed. Fortunately, even with complete corneal denervation, neurotrophic changes do not always occur. Twenty (36.4%) of 55 patients who had undergone surgery for trigeminal neurilemomas[174] demonstrated decreased sensation, but only 5 (9.1%) reportedly developed corneal complications. In the early series of cavernous sinus surgery, trigeminal dysfunction was mentioned in a minority of patients. In the first 7 patients reported, only the third division of the fifth nerve was noted to be affected. Six (14.3%) of 42 patients were said to have temporary, and 3 (7.1%) permanent, loss of sensation in the V_1 distribution.[158] Trigeminal dysfunction was recognized in only 3 (3.3%) of 91 patients following surgery,[175] but in a later review that same year there were 10 (9.9%) of 101 cases. Al-Mefty and colleagues[99] reported on 9 transient (12.2%) and 1 permanent (1.4%) fifth nerve dysfunction among 74 patients who had undergone surgery. The group in Hanover reported 16 (29.6%) of 54 patients with preoperative trigeminal dysfunction, 17 (31.5%) with temporary or partial dysfunction following surgery, and 10 patients (18.5%) with permanent fifth nerve dysfunction.[120] In a more recent review, DeMonte[136] reported 6 (19%) of 31 patients who developed new fifth nerve dysfunction following surgery. Forty-seven (76%) of 62 patients without trigeminal dysfunction preoperatively were noted to have some loss of corneal sensation in our series with more quantitative assessment. This may be more serious given that the fifth nerve seems to have a worse prognosis for recovery, and in the present series 15 patients (32% of those with trigeminal dysfunction) eventually developed neurotrophic keratitis.

The potential for developing neurotrophic keratitis following the loss of fifth nerve function can be exacerbated by several factors. These include loss of tear production, seventh nerve dysfunction with problems in eyelid closure, and problems with ocular motility resulting in the inability to move the eye out of the palpebral fissure. None of these issues has been discussed in any prior neurosurgical series, however. Aggressive lubrication is an essential treatment in patients at risk for neurotrophic keratitis. The use of gold weight implants, tarsorrhaphy, or other protective procedures is probably best completed early when the loss of corneal sensation is associated with decreased seventh nerve function. A vascularization procedure (Gunderson flap) may be required to keep the eye from perforating with recurrent epithelial defects, erosion, or infection. Nerve growth factor treatment may be an additional mode of

therapy in patients with persistent sensory loss.[176,177] Unfortunately, initial studies suggest that patients with surgically induced neurotrophic keratitis are probably the most resistant to treatment.

What Are the Alternative Treatment Options for Patients With Cavernous Sinus Pathology?

In discussing surgery and its consequences, we must compare surgical results to alternative treatment modalities. Radiation therapy has been used to treat neoplasia almost since x-rays were discovered by Roentgen at the turn of the last century. Malignant lesions (especially lymphoproliferative tumors including lymphoma and plasmacytoma) may be very radiosensitive. It was thought that benign slow-growing tumors would respond poorly to radiation. Somewhat surprisingly, the growth rate of meningiomas can be altered with conventional fractionated radiation.[178-180] Regression based on imaging or improvement in cranial nerve function, however, is exceptional. Radiation may play a more active role in other types of skull base tumors. This is particularly true for malignancies but also for chordomas.[181]

Over the last decade an increasing interest has been expressed for the use of radiosurgery. This is defined as a single-dose application, either of a gamma source or through a linear accelerator. Additional smaller studies of the use of proton beam have also been reported for meningiomas involving the cavernous sinus. The development of single-dose focal radiation therapy (LINAC[182,183]) and gamma knife[184-194] has offered additional options. The exact role of these modalities is yet to be defined.[191] Significant series reported on the use of gamma knife have included upward of 1,000 meningiomas involving the cavernous sinus treated either primarily or following subtotal resection.[189,190,192-199] The emphasis has been on "control."[197] Unfortunately, although some of the case follow-ups have been 8 years or more, the majority of series have been limited to 3 to 4 years.[190,197,200,201] Based on previous experience, this is much too early in order to be able to truly assess the effectiveness of gamma knife in these patients.[184-188,190]

While complications have been low, they do occur. Several studies have addressed the potential for radiation optic neuropathy in patients undergoing gamma knife. The optic nerve and the visual pathways are more susceptible to potential radiation damage.[202,203] Some investigators have emphasized the ability to treat lesions directly applied to the optic nerve.[201,204] On the other hand, it has been suggested that optic neuropathy could be as high as 77.8% when the optic nerve received a dose of 15 Gy or more.[205] Therefore, lesions should be situated at least 3 mm away from the afferent visual pathways for safe treatment. The "safe dose" of radiation to the optic nerve is yet to be determined, and this fact argues for a conservative approach.[206] The oculomotor and trigeminal nerves are relatively resistant to radiation therapy.[196,204,207] In spite of this, trigeminal and ocular motor problems have been reported.[208,209]

In order to decrease the chance of damage, several investigators have suggested lowering doses.[204] Others have emphasized the importance of treating the entire tumor to at least a dose of 14 Gy.[210] Because of the restriction of radiosurgery to a limited size, some investigators have continued to advocate fractionated radiation therapy for those tumors that are larger.[191] Because of extremely low morbidity, several investigators still advocate the use of fractionated radiation therapy for cavernous sinus meningiomas in general.[211,212] The use of gamma knife treatment with a particular interest for neuro-ophthalmologists was summarized by Carvounis and Katz in 2003.[213]

During the last 2 decades several medical treatments have been proposed for meningiomas. Unfortunately, data on hormonal therapy[214] and hydroxyurea have been disappointing after initial optimistic reports. At this time there are no proven efficacious therapies for meningiomas beyond surgery and radiation. It is hoped that the recent mapping of chromosomal defects in meningiomas[151-153] will lead to alternative treatments.

In view of the slow progression of parasellar meningiomas, a number of surgeons, including several with significant clinical experience, have advocated a limited approach to these tumors consisting of resection of only the extracavernous portion possibly to be followed with radiation therapy.[72,162,215,216] This offers the advantage of decompressing the optic nerve when involved, reducing the tumor size to something that can be treated with radiosurgery, and most important, limiting the complications of aggressive intracavernous surgery.[217-221] Their attitude might best be summed up by a statement made by Madjid Samii: "Why should we risk a carotid artery and eye function for a lesion that hardly ever endangers the patient's life as long as the tumor part involving other structures such as the brain stem are resected."

CONCLUSIONS

Pathology that affects the cavernous sinus is more common than previously thought, and recognition is largely due to the advent of modern imaging studies. Ophthalmic manifestations remain the most common indication of cavernous sinus pathology, although often patients are diagnosed when imaging studies are obtained for other reasons. The natural history of pathology affecting the cavernous sinus seems largely undetermined. Benign tumors may be asymptomatic for years, but progressive growth is common. Quantitative evaluation of the visual system is imperative to improve our understanding of the true natural history of these lesions. Failure to measure function accurately can lead to erroneous underestimation of the true incidence of dysfunction. Quantitative evaluation is important to direct therapeutic intervention. The timing of rehabilitative surgery depends on the degree of postoperative ocular motor stabilization.

Our study supports the literature that cavernous sinus surgery is technically feasible with relatively low mortality in patients with meningiomas. Nonetheless, quantitative assessment indicates that cavernous sinus surgery only infrequently benefits preexisting cranial nerve dysfunction. The one exception to this rule is extracavernous extension with compression of the optic nerve, which can be benefited by decompression in the area of the orbital apex. One caveat not previously reported in the literature is the danger to the optic nerve posed by the skull base pterional approach, which requires take-down of the anterior clinoid and portions of the optic canal. Although central acuity may remain fairly good, quantitative assessment of optic nerve function may detect a previously

unrecognized postoperative incidence of visual field abnormalities. The mechanism of damage to the optic nerve is unknown, but may be related to the surgical removal of the anterior clinoid, during which there may be heat transfer to the optic nerve or, alternatively, hemorrhage-induced vasospasm. It is also possible that there may be direct mechanical damage to the optic nerve within the canal. Improvement in compromised optic nerve function could be obtained by simply excising the extracavernous portion of the tumor without the inherent risks of surgery within the cavernous sinus proper.

Oculomotor dysfunction following cavernous sinus surgery occurred in 97% of cases. This deficit is transient in the majority, but may also be permanent. The prognosis for complete resolution is better if the cranial nerve palsy is incomplete following surgery. Patients with complete oculomotor dysfunction postoperatively have an 84% chance of partially improved function with time, but a 32% incidence of developing aberrant regeneration, which is not necessarily incompatible with binocularity. Surgeons should discuss the potential for diplopia and the need for extraocular muscle surgery prior to proceeding with intervention.

Trigeminal dysfunction is common. The fact that neurotrophic keratitis can be expected in more than one-quarter of patients argues strongly for the importance of ophthalmic input into long-term follow-up of patients with cavernous sinus lesions. In this way, many of the consequences of neurotrophic keratitis may be prevented, as indicated in the section "Ophthalmic Rehabilitation."

To keep this series uniform, only the results of a single surgeon were analyzed. Additional cavernous sinus surgeries performed by other neurosurgeons were excluded from this study. Although it is theoretically possible that other surgeons could have better results, this particular surgeon had more experience with cavernous sinus surgery than all others present and maintains the largest volume of cavernous sinus procedures. Given that many previously reported procedures were completed at other institutions, it is impossible quantitatively to assess ophthalmic function elsewhere. We can only conclude that more intense scrutiny from a neuro-ophthalmic point of view would reveal a higher incidence of ophthalmic pathology. Because neurosurgeons are not specifically trained to quantitatively assess ophthalmic function, it may be misleading to accept previous papers that report patient improvement based on subjective assessment. It is imperative that patients be presented with accurate data before making decisions with regard to this mode of therapy. With other treatment options potentially available, patients should be fully educated before a decision is made to perform this procedure.

This study would have benefited from a longer follow-up, but because many of the patients were coming from great distances, it was not possible to get them all back for a quantitative assessment. We chose not to accept nonquantitative data reported from other institutions because of the lack of detailed assessment, thus limiting the percentage of long-term follow-up. This is important if definitive statements are going to be made with regard to risk percentages. At this time, however, the thesis that cavernous sinus surgery has low ophthalmic morbidity is not justified. Patients undergoing cavernous sinus surgery can expect to have worsening of cranial nerve function that, even when transient, may leave them with substantial residual problems, including development of neurotrophic keratitis, and evidence of aberrant regeneration, which may produce persistent diplopia. There is a low incidence of improvement in cranial nerve function, and therefore patients should not be promised ocular motor improvement with less diplopia following surgery.

The last 2 decades of surgical refinement in dealing with skull base lesions has largely taught us what we can do. What we should do depends on a frank discussion of the options and a realistic assessment of the risks and benefits of surgery and its alternatives. It is likely that in the future, surgery will once again play a smaller, rather than a greater, role in treating cavernous sinus lesions. A combination of limited surgery and some form of radiation may reduce the morbidity associated with surgical treatment.[195] This course has been suggested and probably represents the current mainstream opinion in neurosurgery. At this time the lack of many other good options will still require the consideration of surgical options, and in the right case, surgery, especially if tailored to a realistic goal, may provide significant benefit to our patients.

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APPENDIX A

For the last 12 years diagnostic files have been kept in a computerized database in the Neuro-ophthalmology Unit at the University of Virginia. A search of the database for patients with cavernous sinus involvement produced 347 records, including 230 women and 117 men with an overall average age at presentation of 51 years. Patients broken down by diagnosis revealed a relatively similar age range across pathology; both vascular and neoplastic lesions presented at a mean age between the late fifth and early sixth decades. When evaluated by subgroups, the carcinomatous lesions tended to appear later with a mean age of 58, while the neurilemomas were diagnosed earliest with a mean age of 31. As opposed to most of the early series published in the pre-imaging era, inflammatory lesions made up a tiny portion of this series. One of the potential problems in the diagnosis of inflammatory lesions prior to the advent of imaging studies was the presumption of inflammation when symptoms remitted with steroid therapy. A course of steroid therapy, in fact, was suggested as a way of diagnosing Tolosa-Hunt syndrome. Spector[222] pointed out the frequency of misdiagnosing inflammatory disease in the setting of neoplasia. In 1986 he reported 4 cases of neoplastic lesions originally diagnosed as having Tolosa-Hunt syndrome. A response to steroids was taken as evidence of inflammation. Unfortunately, it is quite clear that neoplastic processes, especially the lymphoproliferative disorders, but also including meningiomas and other benign tumors, may have some response to steroid therapy with resultant diminution of symptoms and signs. The distinction between inflammatory and neoplastic lesions may be quite difficult, exacerbated by possibility of variation[223] or even spontaneous recovery of a neoplastic induced cranial nerve palsy.[224] Even in the modern era of imaging, neoplasia may sometimes simulate an inflammatory etiology. Only 20 patients were inflammatory or infectious etiologies, including cavernous sinus thrombosis in 4 patients, mucormycosis in 2 patients, and aspergillomas in 3 patients. There were 7 patients with Tolosa-Hunt syndrome, and most of these were diagnosed earlier in the series.

Aneurysm and fistulae continued to make up a large number of the patients within this series, representing 13% and 15% of the total, respectively.

The largest group pathologically was neoplastic. This is dramatically different from the series published between 1922 and 1977.[81,83,86,225] In Rucker’s 1958 series,[226] of 1,000 cases of ocular motor paralysis, neoplasms made up only 17% of the cases. Of those series that had a significant number of mass lesions, malignancy was the most common, especially nasopharyngeal carcinoma with secondary involvement of the skull base. In the most recent large series of cavernous sinus lesions, published by Keane in 1996,[87] tumors made up the largest single group (30%), but the majority were still malignant, including nasopharyngeal carcinoma and metastatic disease. Only 4 cases were meningiomas (9% of the 45 tumors). This was similar to 3 (6%) of 50 cases in Jefferson’s series[83] and 3 (4.3%) of 70 cases in the Mayo Clinic series published by Thomas.[86] As late as 1982, Parkinson[133] still felt that malignancy was the most common tumor involving the skull base.

Malignant tumors still make up a significant percentage of cavernous sinus lesions in our series (48 [13.8%] of 347). Some of these were due to direct extension from the nasopharynx and the paranasal sinuses; more were metastatic or due to neurotrophic

spread. The preponderance of meningiomas in our series reflects a referral bias (in view of the skull base interest at the University of Virginia, Charlottesville) and the true frequency of meningiomas. These numbers are similar to other large surgical series, including those from Pittsburgh,[227] University of Arkansas,[99] and Ljubljana.[98] The other likely reason for the change in frequency relates to the advent of modern imaging studies. Meningiomas affecting the cavernous sinus may be quite indolent with little in the way of symptoms. As the use of magnetic resonance imaging (MRI) and computed tomography (CT) for evaluation of various cranial complaints increases, the number of meningiomas fortuitously discovered will likely increase. Many of the patients in our series were diagnosed when a scan was done to evaluate headaches. Headache and facial pain was the second most frequent symptom in the series of 82 patients evaluated for cavernous sinus surgery (see above).

The other difference between our series and that of Keane was the relative decreased frequency of trauma as a specific etiology. Although several of our carotid cavernous fistulae were traumatic in etiology, trauma as a primary cause of the cavernous sinus syndrome was diagnosed in only one case. This contrasts to Keane's finding of trauma as an etiology in 36 patients, or 24% of his series. His series was drawn from patients presenting to a Level 1 trauma facility. In addition, 17 of Keane's patients had surgical trauma following craniotomy and parasellar surgery.

Another important distinction between this series and Keane's was his requirement that patients demonstrate multiple cranial nerve palsies. In this series patients were included on the basis of radiographic as well as clinical characteristics. Thus, several of the patients in the University of Virginia series had no evidence of ophthalmic or neuro-ophthalmic findings, and only imaging studies indicated involvement. In the earlier portion of our series, many of these patients were diagnosed on CT scan alone, but more recently, patients with cavernous sinus pathology were best evaluated by MRI with the use of gadolinium contrast.

TABLE. FINAL DIAGNOSIS OF PATIENTS CODED WITH CAVERNOUS SINUS LESIONS

Neoplasia	225
Malignant	48
Carcinoma	25
Bone-based tumors	14
Sarcoma	2
Other	7
Benign	177
Meningioma	118
Pituitary	35
Neurilemoma	6
Cavernous hemangioma	6
Other	6
Vascular	97
Aneurysm	45
Fistulae	52
Inflammatory	20
Tolosa-Hunt	7
Thrombosis	4
Aspergilloma	3
Zoster	2
Mucormycosis	2
Sarcoid	1
Granuloma	1
Other	5
Total	347

APPENDIX B

TABLE. PRIOR STUDIES OF CAVERNOUS SINUS PATHOLOGY

PATHOLOGY	JEFFERSON[83]	DOLENC[98]	AL-MEFTY[99]	LANZINO[227]	CURRENT
Neoplasm					
Meningioma	3 (6%)	40 (63%)	42 (27%)	66 (45%)	118 (34%)
Pituitary	11 (21%)	7 (11%)	35 (23%)	8 (5%)	35 (10%)
Neurilemoma	4 (7%)	4 (7%)	4 (2.5%)	12 (8%)	12 (3%)
Carcinoma	31 (60%)		25 (16%)	11 (7%)	39 (11%)
Cavernous hemangioma					6 (2%)
Other	3 (6%)	10 (16%)	12 (8%)	53 (35%)	9 (3%)
Vascular					
Aneurysm			32 (21%)		45 (13%)
Fistula			4 (2.5%)		52 (15%)
Inflammatory					20 (6%)
Other		2 (3%)			11 (3%)
Totals	52	63	154	150	347