Rate of Progression and Severity of Neuro-Ophthalmologic Manifestations of Cavernous Sinus Meningiomas

Abstract—The progression of neuro-ophthalmologic signs and symptoms caused by cavernous sinus meningiomas (CSMs) was evaluated in 24 patients. Ten patients had primary involvement of the cavernous sinus by meningioma, and 14 patients had extension of a sphenoid ridge meningioma into the cavernous sinus. Eighteen patients were followed after intradural meningioma debulking. Two of these patients underwent conventional radiation therapy after surgery. The other six patients were followed without treatment. Optic neuropathy caused by extension of the CSM was the most frequently (67%) seen manifestation at the beginning of the follow-up period. Proptosis (50%), ocular motor nerve palsies (46%), and trigeminal neuropathy (33%) were also common. During a mean follow-up period of 57 months, 14 patients (58%) had no change in neurologic status, four patients (17%) had improvement in one or more parameters and six patients (25%) worsened. The patients who worsened had progression of preexisting cranial nerve palsies (two patients), developed new cranial neuropathies (three patients), or both (one patient). Patients who worsened had a significantly longer mean follow-up (76 months) than patients who remained stable or improved (47 months) ($p = 0.01$). Although the signs and symptoms of CSMs may worsen with time, the rate is slow and the degree is mild. These factors are important when considering treatment options. (*Skull Base Surgery, Volume 2, Number 3, 1992, p. 129*)

Meningiomas may arise within the cavernous sinus (CSM) or extend into it from an adjacent region, such as the medial sphenoid ridge. Signs and symptoms are usually ophthalmologic and result from compression of the intimately associated blood vessels and the ocular motor and trigeminal nerves.¹ In addition the optic nerves are often affected by extension of a primary CSM or by a sphenoid ridge meningioma that has extended to involve both the cavernous sinus and the optic nerve. Thus, the hallmark of CSMs is an ocular motility deficit associated with disturbances of facial sensation and visual loss from optic neuropathy.²

In the past, the anatomic relationships within the cavernous sinus were thought to preclude intracavernous

sinus dissection, and treatment of CSMs was usually limited to removal of the intradural component of the tumor. Thus, radiotherapy has been considered an appropriate alternative in the treatment of CSM.³ Recent advances in equipment and technique have allowed a more aggressive approach to CSMs, with some authors advocating microdissection and extensive removal of tumor from within the cavernous sinus as well as outside it.⁴⁻⁸ However, this procedure is associated with increased morbidity and mortality, and the rate of progression of signs and symptoms caused by CSMs has not been well documented.

We reviewed the charts of 24 patients with CSMs who either were followed without treatment or underwent in-

tradural (extracavernous sinus) tumor debulking, with or without subsequent radiotherapy, to assess the natural history of CSMs. We performed this study to determine if the rate of progression and the severity of signs and symptoms caused by CSMs justifies a more aggressive approach to treatment.

METHODS

A computer search through all records of the Johns Hopkins Hospital from 1975 to 1990 identified 438 patients with the diagnosis of meningioma. A search through the records of the Wilmer Institute's Neuro-Ophthalmology Unit revealed that 248 of these patients had undergone a complete neuro-ophthalmologic examination. Records of 247 of the 248 (99.6%) patients were located and reviewed. Meningioma was present within the cavernous sinus in 33 patients (13%). All patients underwent neuroimaging studies, including computed tomographic (CT) scanning, magnetic resonance imaging (MRI), or both. Nine of these patients were excluded from this study because of inadequate follow-up. The remaining 24 patients are the subjects of this study.

Meningioma was a histologic diagnosis in 18 patients and a neuroimaging diagnosis in six patients. Ten patients had a meningioma located predominately in the cavernous sinus, and 14 patients had a sphenoid ridge meningioma that extended into the cavernous sinus. Eighteen patients had intradural meningioma debulking before the period of follow-up and two of these patients received subsequent radiotherapy (5000 to 6000 cGy over 2 months). The other six patients were followed without treatment. A fronto-temporal bone flap provided access to the tumor in patients who underwent craniotomy. All surgery was performed with an operating microscope. Tumor removal was accomplished using bipolar coagulation, emulsification (Cavitron), sharp dissection, or a combination of these.

During the period of observation, patients underwent neuro-ophthalmologic examination, including evaluation of best-corrected visual acuity, color vision, pupillary responses, visual field, proptosis, ocular motility, and the appearance of the optic disc and peripapillary retinal nerve fiber layer. Color vision was tested with the Hardy-Rand-Rittler pseudoisochromatic plates. Visual fields were evaluated using a Goldmann perimeter. Several patients unable to undergo kinetic perimetry were tested by a confrontation technique described by Miller⁹ and by Trobe et al.¹⁰ Proptosis was measured with a Hertel exophthalmometer. Unilateral optic neuropathy was defined as the presence of a relative afferent pupillary defect unassociated with any other lesion that could explain its presence. An optic neuropathy was considered to have worsened if visual acuity decreased by two or more Snellen lines. Trigeminal nerve dysfunction was considered present if there was a decrease in facial sensation or if facial pain was present in a dermatomal pattern. Abnormalities and

changes in ocular motility were quantitated by orthoptic measurements. Proptosis was defined as more than 2 mm difference in Hertel measurements between an individual's eyes.

RESULTS

There were 21 women and 3 men in this study: a 7:1 ratio. The age range was 19 to 80 years, with a mean age of 56 years. Optic nerve dysfunction was present in 16 patients (67%) and was the most frequently observed neuro-ophthalmologic abnormality (Table 1). Optic neuropathy was thought to be caused by direct effects of the meningioma in 14 of the 16 patients (88%). One patient had postpapilledema optic atrophy, and one patient had undergone intentional optic nerve transection to facilitate a previous debulking procedure. Proptosis and trigeminal neuropathy occurred less frequently (50% and 33%, respectively). Forty-six percent of patients had an ocular motor nerve paresis. The oculomotor nerve was affected most frequently (38%), followed by the abducens (21%) and the trochlear nerves (8%). Multiple cranial nerves were affected in nine patients (38%). Two patients had normal neuro-ophthalmologic examinations at presentation.

The range of follow-up was 7 to 120 months, with a mean of 57 months. There was no radiographic evidence of significant tumor enlargement during the follow-up period. Fourteen of the patients (58%) had no change in their neurologic examination during a mean follow-up of 47 months. Four patients (17%) improved over a mean follow-up of 32 months (Table 2). Two of these patients experienced improvement in unilateral optic neuropathy between 2 and 4 years after surgical debulking and subsequent radiotherapy. The other two patients had undergone no treatment for their tumors. One of them had spontaneous improvement of an optic neuropathy (acuity, 20/50 changing to 20/20), and the other had spontaneous complete resolution of a partial oculomotor nerve paresis.

Only six patients (25%) experienced worsening of preexisting visual deficits, development of new deficits, or

Table 1. Clinical Manifestations at Beginning of Follow-up Period

	Patients	
	No.	%
Optic neuropathy	16	67*
Proptosis	12	50
Ocular motor nerve palsy	11	46
Oculomotor	9	38
Trochlear	2	8
Abducens	5	21
Trigeminal neuropathy	8	33

*One patient had post-papilledema optic atrophy and one patient had transection of the optic nerve at prior surgery.

Table 2. Clinical Status at Most Recent Evaluation

	<i>Never Present</i>	<i>Stable</i>	<i>Better*</i>	<i>Worse</i>	<i>New</i>
Optic neuropathy	7	11	3	1	2
Proptosis	12	12	0	0	0
Ocular motor nerve palsies					
Oculomotor	14	6	1 [†]	2	1
Trochlear	21	2	0	0	1
Aducens	17	3	0	2	2
Trigeminal neuropathy	15	8	0	0	1

*Two patients improved spontaneously, and two improved after surgery.

[†]This patient had spontaneous resolution of a partial oculomotor nerve paresis.

both during the follow-up period. Three patients experienced worsening of preexisting deficits during the follow-up period (Table 2). One of these patients had an isolated optic neuropathy with initial visual acuity of 20/400 that deteriorated to no light perception over 10 years. The other two patients both had ocular motor nerve pareses that worsened over an 8-year period. One of these patients had worsening of a preexisting abducens nerve paresis; the other had worsening of both a preexisting oculomotor nerve paresis and a preexisting abducens nerve paresis.

Two patients developed new deficits unassociated with worsening of preexisting neurologic deficits during the follow-up period (Table 2). One of these patients had stable partial oculomotor and abducens nerve pareses but developed a mild optic neuropathy (acuity, 20/30) over 66 months. The other patient had a stable optic neuropathy but developed oculomotor and abducens nerve palsies over 44 months. Both of these patients also developed aberrant regeneration of the oculomotor nerve.

One patient had worsening of a preexisting visual deficit and developed new deficits during the follow-up period. This patient had worsening of a preexisting oculomotor nerve paresis and also developed new ipsilateral trochlear, abducens, trigeminal, and optic neuropathies over 32 months.

Five of the six patients who worsened or developed new deficits had undergone previous debulking procedures, and one of these five patients also had undergone postoperative radiotherapy. Only one patient had been followed without treatment. The six patients who worsened had a significantly longer follow-up (76 months) than the patients who were stable (47 months) ($p = 0.01$, Student's *t*-test).

DISCUSSION

Meningiomas within the cavernous sinus often cause a variety of neuro-ophthalmologic manifestations. Multiple cranial neuropathies are particularly characteristic of cavernous sinus lesions because of the proximity of the ocular motor, trigeminal, and optic nerves; however, other signs may also occur.² Aberrant regeneration of third nerve fibers can occur after damage caused by a CSM.

Usually, there is a history of an acute third nerve palsy before the development of the aberrant regeneration. Aberrant regeneration that occurs in the absence of a previous acute third nerve palsy is considered "primary" and is most often caused by a slowly growing cavernous sinus or parasellar mass.¹¹⁻¹³ Orbital signs, including proptosis and orbital congestion, may occur when the orbital venous drainage is compromised. Damage to postganglionic oculosympathetic fibers as they traverse the cavernous sinus (Horner's syndrome) occurs,¹⁴ but is infrequently reported, perhaps because the eyelid and pupil are also frequently affected by oculomotor nerve dysfunction.

Treatment of meningioma within the cavernous sinus is controversial. In the past, patients treated surgically underwent debulking primarily of the intradural portion of the tumor outside the cavernous sinus without an attempt being made to remove tumor from within the sinus itself. The extradural (intracavernous sinus) tumor component was left intact to avoid further damage to the cranial nerves and blood vessels (particularly the internal carotid artery) within the cavernous sinus.

Recently, more aggressive surgical approaches consisting of microdissection within the cavernous sinus with more extensive removal of tumor have been performed.⁴⁻⁸ "Complete" removal of tumor has been reported in 71 to 76% of cases in which this approach has been used, but complication rates are higher.^{4,5} Cranial nerve palsies are the most frequent postoperative sequelae, and although they may be transient, permanent deficits are common.^{4,15,16} Golnik and Newman¹⁵ prospectively evaluated oculomotor nerve function before and after direct surgery of the cavernous sinus in nine patients with cavernous sinus meningiomas. Immediately postoperatively, all patients had either worsening or development of third nerve paresis. Within 3 to 10 months after surgery, five of the nine patients had recovered completely without evidence of aberrant regeneration. Patients who developed third nerve paresis postoperatively had more recovery of function and better ocular alignment than patients who developed worsening of preoperative deficits. Dolenc and associates⁴ reported a 19% (12 of 63 patients) incidence of permanent cranial nerve palsies following direct cavernous sinus surgery. However, only 40 of their 63 patients had meningioma, and the authors did not specify compli-

cation rate by tumor type. More catastrophic complications of direct surgery of the cavernous sinus have been reported. Lesoin and associates¹⁷ reported on one patient who developed "complete blindness and ophthalmoplegia" and another who died of "massive cerebral ischemia" secondary to intracavernous carotid thrombosis associated with extreme carotid artery tumor stenosis. Three of the patients in Dolenc et al's⁴ series died in the perioperative period, two from pulmonary emboli and one from myocardial infarction. High recurrence rates following intradural CSM debulking lead many investigators to believe that these surgical complications are acceptable in order to achieve "total" tumor removal. Thus, the benefit of direct cavernous sinus surgery versus intradural debulking procedures cannot be evaluated until recurrence rates can be determined for the direct surgical approach.

Radiotherapy may be used to treat CSMs either as a primary form of treatment or as an adjunct to surgical excision. Primary radiotherapy has been considered an attractive alternative to surgery for "inoperable" cavernous sinus meningiomas. Van Effenterre and associates³ irradiated eight such patients. Each of these patients had improvement in cranial nerve palsies, with three patients experiencing total resolution. Primary radiotherapy of meningiomas in other intracranial locations has produced variable results.¹⁸⁻²¹ Radiotherapy as an adjunct to surgical excision of meningiomas has been used because of reports of high recurrence rates. CSMs have not been specifically evaluated, but recurrence rates for intracranial meningiomas after adjunctive radiotherapy are encouraging.²¹⁻²⁴

Stereotactic radiosurgery may be efficacious in the treatment of CSMs. Kodziolka and associates²⁵ treated 50 patients with meningiomas, 13 of whom had CSMs, with a 201-source cobalt-60 gamma knife and reported no immediate postoperative complications. Sixteen of these patients received primary radiosurgery, and the others were treated after surgical debulking. No worsening or development of cranial nerve palsies occurred during a follow-up period that ranged from 6 to 30 months.

The risk-benefit ratio of any form of treatment for CSM is difficult to assess without knowledge of the natural history of meningiomas in this location. Unfortunately, there are few reports of the natural history of CSMs. Trobe and associates¹² reported on seven patients with CSMs who presented with ptosis, diplopia, or both. These authors commented that "these symptoms were so well tolerated that medical attention was only sought after an interval of 8-60 months." After presentation, three of the patients were stable over 10 to 36 months, three patients had mild worsening of their ophthalmoparesis over 8 to 44 months, and one patient developed an optic neuropathy after 31 months. Other investigators have also reported either mild worsening of neuro-ophthalmologic signs and symptoms over 2 to 20 years,^{13,26-28} or stability for up to 17 years.¹³

We followed a group of patients with CSMs to docu-

ment any changes in neuro-ophthalmologic signs over a follow-up period ranging from 7 months to 10 years. The majority of our patients were either stable or experienced *improvement* (75%) over a mean follow-up of 47 months. Several of these patients were stable for 8 years. Two of four patients experienced improvement in an optic neuropathy after surgery. Presumably, the improvement occurred because of decompression of the optic nerve even though improvement occurred 2 to 4 years after surgery. However, the other two patients improved *spontaneously* without treatment.

Only six of our patients with CSMs experience gradual worsening of signs and symptoms over 32 months to 10 years and only two of these patients were significantly affected by these changes. One patient initially without diplopia developed oculomotor and abducens nerve pareses, and another patient with only mild oculomotor nerve dysfunction at presentation developed trochlear, trigeminal, abducens, and optic neuropathies. The other four patients who clinically worsened but were symptomatically stable, either experienced worsening of preexisting ophthalmoparesis and had persistent diplopia or had further optic nerve damage in an eye with severe visual loss at presentation.

It is apparent that CSMs produce variable rates of progression of signs and symptoms. Firsching and associates²⁹ analyzed serial CT scans or MRI images and found the annual growth rate of intracranial meningiomas to vary from less than 1 to 21%.²⁹ This wide range of growth rates may help to explain the variable rates of progression of signs and symptoms caused by CSMs. We await long-term data comparing patients with CSMs treated by intradural debulking, direct surgery of the cavernous sinus, or primary radiotherapy, so we can assess the risk-benefit ratio of each therapy in relation to the natural history of these tumors. In the meantime, the slow progression of signs and symptoms caused by CSMs must be contrasted with the potential morbidity and mortality of aggressive surgery. Patients should be warned that symptoms may slowly progress and that surgical treatment, particularly microdissection within the cavernous sinus, is not a necessity.

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REVIEWER'S COMMENTS

Golnik et al have provided valuable information on the behavior of meningiomas involving the cavernous sinus, although histologic verification was not obtained in all cases. The authors provide evidence that the biologic behavior of these lesions is often quite benign. Although I share a similar impression regarding the growth of intraorbital meningiomas or those involving the cavernous sinus, it would be interesting to ascertain the outcome of the nine patients for whom adequate follow-up could not be obtained, since this information could significantly affect the author's conclusions. Nonetheless, the data provided should be helpful in the decision-making process when determining what therapeutic approach will be taken by patients and surgeons confronted by meningiomas primarily involving the cavernous sinus. Issues that must also be addressed include the effect of age at diagnosis, hormonal status, and outcome after intervention because of disease progression versus outcome when therapy is undertaken at the time of presentation. In addition, it will be important to assess the role pharmacologic manipulation with agents such as RU 486 will play in the management of these lesions. I agree that it is important to determine the natural history of meningiomas of the cavernous sinus, since treatment entails significant risks for our patients. We must continue to look for characteristics that will predict which patients will progress or require intervention. Golnik et al have taken an excellent step toward providing this information.

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