Update on treatment modalities for optic nerve sheath meningiomas

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Optic nerve sheath meningiomas (ONSMs) represent 1 to 2% of all meningiomas and one third of all optic nerve tumors. The management of ONSMs is controversial. Traditional surgical removal often results in postoperative blindness in the affected eye and thus has been abandoned as a treatment option in most patients. Surgery may be unnecessarily aggressive, especially if the patient has useful vision. When these tumors are left untreated, however, ensuing progressive visual impairment may lead to complete blindness. More recently, radiotherapy has gained wider acceptance as a treatment for these lesions. The authors of some reports have suggested that fractionated stereotactic radiosurgery (SRS) may be the best option for treating primary ONSMs. In patients with documented progressive visual deterioration, fractionated SRS may be effective in improving or stabilizing remaining functional vision. The authors review the clinical presentation, radiographic characteristics, and management of ONSMs, emphasizing the use of fractionated SRS.

KEY WORDS • optic nerve sheath meningioma • benign • stereotaxy • radiosurgery • dose fractionation • orbital neoplasm

Meningiomas involving the optic nerve and the anterior visual pathways have intrigued neurosurgeons and ophthalmologists for nearly a century. The first definitive case of an ONSM was described in 1936.⁶ By 1938, the potential had been demonstrated for removal of these tumors by complete excision of the optic nerve involving the tumor.⁷

Optic nerve sheath meningiomas account for 1 to 2% of all meningiomas, 1.7% among orbital tumors, and are the second most common optic nerve tumor after optic gliomas.^{7,9,15,30,37} These tumors typically affect middle-aged women and present with progressive visual loss. Most ONSMs are unilateral; only 5% are bilateral. There is no strong evidence for right or left laterality.⁹

Optimal treatment of ONSMs remains undefined.^{12,15} Conservative treatment can be considered because of the indolent growth pattern of these tumors and the extremely low mortality rates associated with them. Over time, however, deterioration of vision always occurs. Traditional excision almost always results in postoperative

blindness to the affected eye because of the intimate circumferential relationship of the optic nerve and the central retinal artery. Although a few authors have reported rare cases of improved vision after resection,^{1,5,10,23} surgery offers no benefit to most patients with ONSMs and should be reserved for those in whom blindness, severe proptosis, or intracranial involvement has developed.^{9,15}

Radiotherapy of intracranial meningiomas has long been known to reduce recurrence and tumor progression.^{17,18,35,36} In the last decade, conventional radiotherapy has been used to treat ONSM, and visual function has improved in 75% of cases.^{9,14,15,31} The complications of radiation-induced optic neuropathy and radiation necrosis, however,^{4,26,28} led to the search for better radiation-delivery techniques. The advent of 3D conformal radiotherapy and SRS has allowed administration of higher-dose radiation to a more specific target, sparing unnecessary radiation to neighboring structures.^{8,11,16,20} Stereotactic radiosurgery involves using a single, high dose of radiation, which may be toxic in the treatment of ONSMs.³³ Fractionated SRS involves similar computer-image integration, but with a relocatable frame that facilitates a staged dosing scheme. This technique allows radiation to be administered with a high degree of accuracy at a dose-per-

Abbreviations used in this paper: CT = computerized tomography; MR = magnetic resonance; ONSM = optic nerve sheath meningioma; SRS = stereotactic radiosurgery; 3D = three-dimensional.

fraction known to be associated with a low risk of radiation-induced optic neuropathy.^{2,8,12,22,29}

The authors of recent reports have demonstrated the potential efficacy of fractionated SRS in preserving or improving vision in patients who harbor ONSMs and who experience progressive visual loss.^{2,12,20,22,25} Known radiobiological concepts explain how a fractionated therapeutic regimen can arrest tumor growth while minimizing radiation-related toxicity to the optic nerve. We review the clinical presentation and radiographic/neuroimaging characteristics of ONSMs and discuss their management with fractionated SRS.

CLINICAL PRESENTATION

In a review of the literature, Dutton⁹ reported the mean age of patients with ONSMs at presentation to be 40.8 years (range 2.5–78 years) with a female predominance (61%). Most ONSMs are unilateral; only 5% of cases are bilateral (Fig. 1).

The triad of progressive painless visual loss, optic nerve atrophy, and opticociliary shunt vessels is almost pathognomonic for the diagnosis of ONSM.³² The simultaneous manifestation of all three signs and symptoms, however, is rare. The most common presenting symptom is progressive loss of visual acuity or visual field (96% of cases). Although long-term survival is likely, in most patients there is gradual progression to complete blindness in the involved eye if the tumor is left untreated. Transient visual obscurations, which may be gaze evoked or spontaneous, may precede, follow, or occur simultaneously with visual loss.^{30,38} Dyschromatopsia and afferent pupillary defects are other common manifestations of ONSM-induced optic neuropathy. The most common visual field defect is peripheral constriction.^{9,30} Other visual field defects, however, such as central or cecocentral scotoma, altitudinal defects, and enlargement of the blind spot, can manifest in compressive optic neuropathy. Patients with ONSM may also have optic disc abnormalities (98%), proptosis (59%), and opticociliary shunt vessels (30%).⁹ Early stages of compressive neuropathy usually manifest as optic disc edema, which may eventually progress to optic atrophy. Opticociliary shunt vessels are a late sign of compressive optic neuropathy. They are presumed to be

Fig. 1. Gadolinium-enhanced and fat-suppression MR images (axial [left] and coronal [right]) obtained in a patient with bilateral ONSMs. The left ONSM has enveloped the optic nerve circumferentially, and the characteristic doughnut sign can be observed. The right ONSM can be seen on the superomedial aspect of the right optic nerve.

collateral vessels that develop between the retinal and choroidal venous circulation to allow blood to bypass the site of compression at the optic nerve.^{12,32}

RADIOGRAPHIC/NEUROIMAGING CHARACTERISTICS

Before the age of CT scanning and MR imaging, the diagnosis of ONSM was difficult. Advances in neuroimaging have allowed the diagnosis of ONSM to be made on the basis of clinical and radiographic findings, thus obviating the need for obtaining a tissue biopsy sample.^{1,9,12,15,21} Early detection of ONSM is essential to prevent intracranial involvement, which may change the course of management.

On neuroimaging studies, ONSMs appear as a diffuse fusiform or tubular enlargement of the optic nerve. They are classified as intraorbital, intracanalicular (optic canal), or intraorbital with intracranial extension (Fig. 2).²¹ The tumor typically surrounds the optic nerve and results in a concentric thickening of the optic nerve diameter. Computerized tomography scans may demonstrate calcification of the nerve sheath or enlargement of the optic canal (Fig. 3). Axial CT scans reveal “tram tracking,” a radiographic sign caused by the density difference between the thicker nerve sheath tumor and the residual optic nerve, which is characterized by central lucency (Fig. 3).⁹ On coronal CT scans, the tumor appears as a “doughnut,” with the dense nerve sheath tumor encircling a central radiolucent optic nerve (Figs. 1–3).¹² Gadolinium-enhanced and fat-suppression MR imaging can precisely

Fig. 2. Gadolinium-enhanced axial (upper) and coronal (lower) MR images demonstrating a left ONSM that extends intracranially into the cavernous sinus.

Fig. 3. *Upper:* Axial CT scan demonstrating calcification along the right optic nerve in a patient with an ONSM. *Center and Lower:* Axial (*center*) and coronal (*lower*) Gd-enhanced and fat-suppression MR images, demonstrating an ONSM arising from the right optic nerve. “Tram tracking” can be seen on the axial CT scan and MR image.

detect and demarcate ONSMs, especially those with an intracanalicular or intracranial component.²¹ The precision of imaging allows for great accuracy during treatment planning with fractionated SRS.

MANAGEMENT: SURGERY AND RADIOTHERAPY

Surgical Management

Cushing and Eisenhardt⁷ first described the resection of the entire optic nerve as a treatment for ONSMs in 1938. Surgical treatment became common, although continued attempts were made to resect the tumor while leaving the nerve intact.^{1,14,23,38}

Attempts at excision of ONSMs may result in significant or total loss of remaining vision because most are located at or near the orbital apex and share their blood supply with the pia mater.^{13,15,16,38} En bloc resection in-

volving removal of the optic nerve may be the best strategy in patients in whom functional vision is lost, especially if there is extensive intracranial extension.^{5,24} Resection may also play a role if the patient suffers from disfiguring proptosis and blindness. A craniotomy is performed to remove tumors that extend intracranially, and orbital exenteration is performed for orbital invasion beyond the optic nerve.¹ The continued recommendation for resection in younger patients, in whom ONSMs may be more biologically aggressive, is highly controversial. These patients may be offered resection of both tumor and optic nerve from the chiasm to the globe, even when vision is functionally good.³⁸ Rare cases of visual improvement after successful tumor resection have been reported.^{1,5,10,12,23}

Optic nerve sheath meningiomas are not uniform in anatomy or presentation. The few that remain extradural, arising from intraorbital arachnoidal rests and secondarily involving the optic nerve,²⁴ can be removed without injury to the optic nerve. True primary ONSMs, in contrast, do not arise from the external surface of the nerve but rather from the area between the arachnoid and the dural sheaths of the optic nerve or from the intracranial cavity growing into this space. They usually wrap circumferentially around the optic nerve and extend posteriorly into the annulus of Zinn. Therefore, most ONSMs may not be completely resected without compromising the integrity of the optic nerve.

Radiation Therapy

Radiation therapy in the treatment of patients with ONSMs has gained wider acceptance in the past decade.^{4,9,18,31,34} Initial treatment with conventional radiotherapy resulted in visual improvement in nine of 12 patients.^{9,14,28,31} These techniques, however, expose the visual apparatus and neighboring tissues to large volumes of radiation, which may cause radiation necrosis and damage.^{4,18,28} Newer modalities, such as 3D conformal radiotherapy and fractionated SRS, use multiple beams of radiation to focus and shape accurately treatment to the lesion, thereby limiting exposure of adjacent normal tissue to damaging radiation.^{2,12,20,22,25} It is known that the optic nerve tolerates a dose per fraction of 1.8 Gy to a total dose

Fig. 4. Representative fractionated SRS dose plan. The tumor can be visualized in relation to the radiation volume and fall off.

TABLE 1
Summary of data obtained in five patients with ONSMs

Case No.	Age (yrs), Sex	Affected Side	Presentation	Visual Acuity	Outcome	Follow-Up Length (yrs)
1	63, F	lt	visual field & acuity loss	20/40	20/30, improved visual field, acuity & color vision	3
2	40, F	lt	visual loss, orbital pain, proptosis, headache	20/30	20/30, stable visual exam	2
3	50, F	lt	visual field loss	20/20	20/15, improved visual field & acuity	1
4	60, M	lt	visual field loss/change in color vision	20/20	20/20, improved visual field & color vision	7
5*	73, M	bilat	blind (lt side), visual field & acuity loss (rt side)	20/40 (rt)	20/30 (rt), improved visual field & acuity	2

* This patient presented with a left ONSM with intracranial extension and involvement of the right optic nerve. Because of the left eye blindness and remaining function in the right eye, fractionated SRS was performed to treat only the right eye.

of 54 Gy or a single dose of 6.5 to 8 Gy.^{19,26,33} Fractionated SRS maximizes the chance of vision preservation while minimizing the risk of radiation-induced optic neuropathy or optic neuritis (Fig. 4). Analysis of data gathered early in the use of fractionated SRS suggests that it effectively improves or stabilizes remaining functional vision in the subset of patients with ONSMs who present with documented progressive visual deterioration.^{2,3,12,20,22,25,27}

In five patients harboring ONSMs, we administered fractionated SRS of 1.8-Gy fractions to a cumulative dose of 45 to 54 Gy, without complications of delayed optic neuropathy (Table 1).²² All patients presented with progressive visual loss involving decreased visual fields, visual acuity, and color vision. We used a dedicated linear accelerator-based radiosurgical technique that involved a conventional fractionation protocol. Patients were fitted with the Gills-Thomas-Cosman relocatable frame (Radionics, Inc., Burlington, MA) and underwent stereotactic CT scanning and/or fat-suppression Gd-enhanced MR imaging. Treatment planning was performed using X-Knife 3D treatment planning software (Radionics). Treatments were planned to encompass the tumor at the 90% isodense line.

Within 3 months after treatment, four of the five patients experienced dramatic improvement in visual func-

tion (Fig. 5). Visual field deficits resolved in all four, visual acuity improved in three, and color vision improved in two. Of the four patients whose visual field deficits resolved, one patient experienced resolution of opticociliary shunt vessels. Optic nerve atrophy and optic disc swelling, however, remained unchanged. In the fifth patient, stabilization of all visual functions occurred. Serial CT and MR images obtained during the follow-up periods revealed the size of the tumors in all five patients to be unchanged from baseline.

In another study,² 33 optic nerves in 30 patients with ONSMs were treated with a similar fractionated SRS protocol (1.8-Gy fractions to a total of 50 to 54 Gy). Of the 24 eyes with preserved useful vision, 92% demonstrated either stability (50%) or improvement (42%) in visual acuity and field testing. Tumor volume was reduced in four patients (13%), and in the remainder there was no evidence of tumor progression or recurrence. Compared with patients who underwent observation, there was a 150% greater probability of visual improvement in the treatment group. In a third study,²⁷ 15 patients were treated and stable or improved vision occurred in all. Collectively, the use of fractionated SRS to treat patients with some residual vision has been successful in stabilizing (22 [47%] of 47) or improving (23 [49%] of 47) vision in nearly all cases (Table 2).

Fractionated SRS appears to confer tumor control and visual improvement or preservation of residual function. The risks of delayed optic neuropathy and secondary malignancies remain unknown, because there is limited long-term follow-up information.^{19,33} Fractionation of the dose and precise targeting, however, will likely reduce the risk of radiation injury of the optic nerve. Fractionated SRS may be the treatment option of choice for patients with ONSMs if vision preservation is the goal.

CONCLUSIONS

In patients harboring ONSM in whom functional vision remains, especially in the early stages of tumor growth, we recommend fractionated SRS to achieve vision stabilization or improvement and tumor control. Because meningiomas can recur slowly many years after excision, the true durable effects of fractionated SRS await longer follow-up study. Early visual improvement, however, should not be ignored even if visual symptoms recur or the tumor enlarges at a later date. Treatment with fractionated

Fig. 5. Visual field testing results obtained in a 50-year-old woman with a left ONSM who presented with visual field loss. Prior to fractionated SRS treatment (Pre-SRT), the visual field test demonstrated diffuse and temporal depression of the left eye. After 30 1.8-Gy fractions (total dose 54 Gy) (Post-SRT) were delivered to the left ONSM, visual field testing showed dramatic improvement of the previous visual field defect.

TABLE 2
Cumulative analysis of stereotactic radiosurgical treatment of ONSMs

Authors & Yr	No. of Cases	Dose/Fraction (Gy)	Total Dose (Gy)	No. of Cases		
				Improvement	Stabilization	Complications
Lee, et al., 1996	1	1.8	50.4	1	0	0
Fineman & Augsburger, 1999	1	1.8	54	0	1	0
Moyer, et al., 2000	1	1.8	50.4	1	0	0
Andrews, et al., 2002	30	1.8	50–54	10*	12*	4
Liu, et al., 2002	5	1.8	45–54	4	1	0
Pitz, et al., 2002	15	1.8	54	7	8	0
total	53			23	22	4

* Of 24 eyes with preserved useful vision.

SRS does not limit later treatment options, as it might in other tumor entities, because complete optic nerve excision or orbital exenteration will likely be undertaken if surgery is performed. Stereotactic radiosurgery may also reduce the risk of radiation injury compared with conventional irradiation modalities.

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