New Concepts in the Management of Optic Nerve Sheath Meningiomas
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Abstract

Introduction: Primary optic nerve sheath meningiomas (ONSMs) are the most common primary tumours of the optic nerve sheath. The diagnosis and management of ONSMs have changed dramatically in the last decade. In this review article, we discuss the latest information regarding these issues. Materials and Methods: References for this manuscript were obtained by searching the database PubMed using the phrase “optic nerve sheath meningioma”. Approximately 150 articles were identified and reviewed. These articles served as reference sources for other articles, books and chapters on the subject. The results were combined with our personal experience, which includes over 100 cases of ONSMs that have been observed or treated with one or more of the modalities described below. Results: The diagnosis of ONSM can be suspected in most cases from clinical findings and supported by the results of neuroimaging, obviating tissue biopsy in the majority of cases. Management depends on several factors. Observation may be appropriate in patients with mild or no visual deficit or in whom visual loss is not progressing, whereas stereotactic fractionated radiation therapy has been documented to improve or stabilise vision in progressive or advanced cases. Attempts at excision of ONSMs are associated with a high risk of blindness and should be reserved for the rare case of an anteriorly located, primarily exophytic tumour with focal involvement of the dural sheath. Rare patients with acute visual deterioration may benefit from optic nerve sheath fenestration. Conclusion: The majority of ONSMs can be suspected on clinical grounds and diagnosed with readily available non-invasive neuroimaging. Stereotactic fractionated radiotherapy is currently the treatment of choice for ONSMs that require therapy.

Key words: Meningioma, Optic nerve, Optic nerve sheath, Radiotherapy

Introduction

Optic nerve sheath meningiomas (ONSMs) account for one-third of primary optic nerve tumours, are the second most common optic nerve tumours after gliomas, and are the most common tumours of the optic nerve sheath.1 Although ONSMs are said to comprise 1% to 2% of all meningiomas, their reported incidence has increased since the development of more advanced neuroimaging techniques, which have also significantly contributed to earlier recognition of the disease.

ONSMs may be primary or secondary. Secondary ONSMs arise intracranially from dura on or near the planum sphenoidale and spread anteriorly within the confines of the optic nerve sheath through the optic canal to surround the orbital portion of the nerve, whereas primary ONSMs arise from arachnoid cap cells within the dural sheath surrounding the orbital or, less commonly, the canalicular portion of the optic nerve.2,3 In this review, we address issues that relate equally to both primary and secondary ONSMs except for those tumours that include an obvious midline soft-tissue mass on the planum sphenoidale.

Independent of the primary site of origin, ONSMs usually spread around the optic nerve through the subdural and subarachnoid spaces, following pathways of least resistance such as vessels and dural septa.2,4 As they spread, they compromise the function of the nerve by impairing blood supply to the nerve and by interfering with axon transport. The tumours thus are interposed between the nerve substance and its extradurally derived blood supply (Fig. 1), making the majority of ONSMs not amenable to resection.

Some ONSMs remain localised to a small segment of the optic nerve, whereas others spread to surround the entire length of the orbital and canalicular portions of the nerve. Rarely, the tumour infiltrates the dura and spreads beyond the confines of the nerve to infiltrate...
adjacent orbital structures, including fat, extraocular muscles, and bone. When the tumour spreads to adjacent bone, it may enter the Haversian canal system, inciting hyperostosis and bone proliferation.5

In a meta-analysis by Dutton published in 1992,1 the mean age at presentation for ONSMs was 41 years (range, 3 to 80), with women being affected more frequently than men (3:2). Patients with neurofibromatosis had a higher incidence of ONSM compared with the general population. Almost all cases (95%) were unilateral. The majority of ONSMs were intraorbital, with 8% confined to the optic canal. Interestingly, canalicular meningiomas had a higher incidence of bilaterality (38%) than ONSMs within the orbit. In a subsequent series reported by Saeed et al in 2003,6 half of the patients with bilateral ONSMs had tumours along the planum sphenoidale in continuity with the lesions in both optic canals. Thus, it would appear that some cases of apparently bilateral ONSMs are truly bilateral, whereas others represent either the spread of a planum sphenoidale meningioma to both optic canals or of a unilateral ONSM across the planum to the contralateral optic canal.

Approximately 4% to 7% of ONSMs occur in childhood. Unlike ONSMs that occur in adults, there is no gender predilection, and they are often associated with neurofibromatosis type 2. In addition, ONSMs in children often behave in a more aggressive fashion characterised by faster growth, and more frequent intracranial and bilateral involvement than occurs in adults.6

Clinical Manifestations

The majority of ONSMs present with a slowly progressive optic neuropathy characterised by a variable loss of visual acuity.1,6-8 In the study performed by Dutton,1 45% of patients had vision of 20/40 or better whereas fewer than 25% had counting fingers or worse. Even patients who do not have significant reduction in visual acuity often have disturbances of colour vision and visual field defects. Less common symptoms in patients with ONSMs include pain or discomfort, double vision, and transient visual obscurations.1,6-8 The obscurations of vision are almost always associated with optic disc swelling and in some cases are exacerbated or induced by eye movement.

Almost all patients with a unilateral ONSM have an ipsilateral relative afferent pupillary defect, and most have either swelling of the optic disc without haemorrhages, exudates or optic atrophy.1,6-8 Other ophthalmoscopic findings include macular swelling contiguous with a swollen optic disc, choroidal folds, and acquired retinochoroidal shunt vessels (Fig. 2). Indeed, the triad of visual loss, optic atrophy, and retinochoroidal shunts is almost pathognomonic for ONSM, although this triad tends to occur relatively late in the course of the disorder.9 Orbital signs such as proptosis are present in 30% to 65% of patients with ONSMs, depending on the series.1,6 Mechanical restriction of ocular motility is found in 39% of patients6 but is usually asymptomatic.

Imaging Modalities

The diagnosis of an ONSM may be made by a variety of imaging studies, most often high-resolution computed tomographic (CT) scanning,10 thin-section magnetic resonance (MR) imaging,11 or ultrasonography.12 These studies generally obviate the need for tissue biopsy in most cases, making an early diagnosis possible without potentially damaging the optic nerve during surgery. Nevertheless, metastatic infiltration of the optic nerve and optic nerve sheath,13,14 as well as lymphoma15 and inflammatory lesions, such as sarcoid,16,17 and sclerosing orbital inflammation18 may mimic ONSMs, and these should be considered in the differential diagnosis of a patient with a presumed ONSM.

ONSMs have 3 main morphologic patterns on imaging: tubular, fusiform, and globular.6 CT scanning typically shows enlargement of the optic nerve with an increased density peripherally and decreased density centrally (the “tram-track” sign).19 These changes are particularly well seen after intravenous injection of iodinated contrast material (Fig. 3). In addition, in some cases of ONSM, calcifications surrounding the nerve are present on CT scanning, although they may be masked by contrast enhancement and thus are best identified on pre-contrast soft-tissue and bone-windowed images.10 The presence of such calcifications is thought to indicate slow growth.5

MR imaging provides somewhat better detail of ONSMs than does CT scanning (Fig. 4).21 In particular, the soft-tissue component of the tumour is readily visible, particularly when T1-weighted images are viewed after intravenous injection of a paramagnetic contrast agent and fat saturation techniques are used. The appearance of the optic nerve on coronal MR images after gadolinium is most often that of a hypodense area (the nerve) surrounded by an enhancing thin, fusiform, or globular peripheral ring of tissue (the tumour) (Fig. 5). In addition, on careful examination, rather than having a perfectly smooth outline, all forms of ONSMs can be seen to have very fine extensions into the orbit (Fig. 6). MR imaging also provides sufficient tissue detail that one can use to assess intracranial extension (Figs. 4 and 6).1,6,11

Ultrasound of the orbit can also be helpful in the diagnosis of an ONSM. Echographic evaluation of an ONSM characteristically shows an enlargement in the diameter of the nerve, with predominantly medium-high reflectivity, and an irregular acoustic structure. In addition, there may be shadowing from internal calcification.1 In many cases,
performance of a 30-degree test reveals solid thickening of the nerve, whereas in others, the tumour is located more posteriorly, and the anterior enlargement of the nerve is due to cerebrospinal fluid that is trapped by the tumour.\textsuperscript{12}

In rare cases, small tumours located within the optic canal are impossible to detect using current neuroimaging procedures. Such lesions are usually discovered during
exploratory craniotomy. The lesions may be suspected, however, in any patient with slowly progressive, unilateral loss of vision associated with signs of optic neuropathy. In addition, the presence of enlarged, aerated, posterior ethmoid and sphenoid sinuses, a condition known as pneumosinus dilatans, is believed by some authors to be pathognomonic of an ONSM.20

**Histology**

Two histological patterns are seen in ONSMs.21 In the meningotheial or syncytial pattern, polygonal cells are arranged in sheets separated by vascular trabecula. Mitoses are uncommon. In the transitional pattern, spindle or oval cells are arranged in whorls. Psammoma bodies are common in this form, and develop from hyalinisation and deposition of calcium salts in the degenerated centres of the whorls.

**Management**

Traditionally, ONSMs have either been observed without intervention or treated by excision of the tumour along with the nerve because of concern for intracranial extension. In such cases, the patient is blind following surgery, and disturbances of eyelid function and eye movements are often present.1 Attempts to excise these tumours while keeping the optic nerve itself intact are usually unsuccessful, and most patients are blind in the eye following such surgery.26,22,24 The only exceptions are ONSMs that are primarily extradural.1 In such cases, the bulk of the tumour can be excised,25 although rarely if ever can the entire tumour be removed,1,6 as at least some of the tumour remains behind in the subdural or subarachnoid space surrounding the nerve. In other cases, particularly those with acute visual loss, some authors recommend opening the optic nerve sheath to decompress the nerve.6,26

To date, trials of medical therapy for ONSM have not been successful. Because meningioma cells often express a variety of hormone receptors, most commonly oestrogen and progesterone receptors,27 it might be expected that treatment with oestrogen or progesterone antagonists would result in the destruction of the tumour or at least a reduction in its size and extent, but this does not seem to be the case. Similarly, although hydroxyurea has been said to be helpful in some cases of intracranial meningioma, we are aware of only one case report in which the treatment of an ONSM with hydroxyurea resulted in visual improvement.28

Radiotherapy for ONSM was initially utilised only as an adjuvant to surgery, as meningiomas in general were once considered to be completely radioresistant. In 1981, however, Smith et al29 reported the successful treatment of 5 patients with ONSMs using conventional fractionated radiotherapy. These authors documented improvement in visual acuity in 2 of the patients, an improvement in the visual field in 3, and regression of retinochoroidal shunt vessels in 2 patients. Kennerdell et al30 subsequently treated 6 patients with fractionated radiation therapy and documented improvement in visual acuity and visual fields in 5 patients with stabilisation in 1. No complications were observed during a follow-up period that ranged from 3 to 7 years.

In 2002, Turbin et al30 reported a retrospective series of 64 patients with ONSMs who had been managed with either observation alone, surgery, surgery with radiation or radiation alone. The study included patients from the original paper by Kennerdell et al.23 The follow-up in this study ranged from 51 months to 516 months, with a mean follow-up of 150 months. Turbin et al concluded that treatment with radiation alone resulted in the best long-term visual outcome even though about one-third of patients treated in this fashion developed complications from the radiation, including radiation retinopathy, retinal vascular occlusion, persistent iritis, and temporal lobe atrophy. The study does not describe which radiation technique was used, but given the era during which the study was conducted and the length of time the patients were followed, it is likely that the majority of the patients were treated with conventional treatment techniques.

The major concern with radiotherapy for ONSMs is late toxicity. Not only can radiation damage the optic nerve itself, but adjacent tissues can also be damaged, including the retina, pituitary gland, and the white-matter tracts of the brain.31 Retinal injury has been described with exposures of more than 50 Gy,32,33 but the coexistence of diabetes mellitus may lower the threshold for retinal or optic nerve damage to 45 Gy.33,34 Late pituitary dysfunction is a rare complication of radiation, as is small-vessel injury in the anterior temporal lobe after irradiation of ONSMs that extend intracranially.33,35

The threshold for radiation damage to the optic nerve, optic chiasm, or both has been estimated to be 8 Gy to 10 Gy for a single dose.34 Because lower doses of radiation are thought to have a more uncertain effect on benign tumours such as ONSMs, and a large, single dose of radiation is associated with a high risk of tissue damage,36 single-dose stereotactic radiosurgery is not widely used to treat ONSMs.35,38 However, stereotactic fractionated radiotherapy (SFR) appears to offer the potential for delivering a sufficient amount of radiation to an ONSM in a manner more focused than that of conventional fractionated radiation therapy, thus minimising the complications from exposure of the surrounding tissue to high doses of radiation.

SFR requires complex planning, which is facilitated by sophisticated software and three-dimensional imaging. The pretreatment imaging (CT and/or MRI) and radiation delivery require the patient to be repeatedly immobilised,
although the newest linear accelerator (LINAC) units such as the Cyberknife use a tracking system that eliminates the need for rigid immobilisation during the treatment phase. Unlike conventional radiation therapy, the LINAC system delivers the radiation in non-coplanar fields that take into account the characteristics of the surrounding tissue. Every beam is size- and shape-adjusted by different devices, micro-leaf collimators being the most advanced way of achieving a high degree of conformality to the tumour, thus minimising irradiation of the surrounding tissue.\textsuperscript{39}

In 1996, the first case report\textsuperscript{40} appeared in the literature documenting improvement of vision after conformal irradiation of ONSM. Since then, at least 7 series have been published that have documented either improvement or stabilisation of vision after SFR. These series are discussed in detail below.

**Current Treatment Options**

**Observation**

The natural history of the ONSM is loss of visual acuity that progresses slowly in most patients over many years.\textsuperscript{6-8,41} ONSMs are not associated with any mortality or neurologic morbidity, and they do not metastasize. Thus, their only effect is on visual sensory function. In a series reported by Narayan et al,\textsuperscript{42} 6 of 7 patients with initial visual acuity of 20/40 or better who were followed without intervention had nearly complete loss of vision over an average duration of 9 years. Nevertheless, observation is appropriate if there is no significant visual dysfunction, no significant progression of visual loss, or no significant intracranial extension of the tumour. In such cases, a clinical examination, including assessment of visual acuity, colour vision, and visual fields should be conducted twice a year for 2 to 3 years, then once a year if the patient’s visual function has remained stable. Patients should be counselled to contact their physician if they note any visual loss in the interim. Neuroimaging at 6-month intervals is appropriate for the first 1 to 2 years, then once a year for 2 to 3 years and then every 3 to 4 years, assuming that the clinical examination is stable.\textsuperscript{43,44} Because younger patients are more likely to have larger or more rapidly developing tumours, children and young adults with presumed ONSMs should be followed both clinically and with neuroimaging at more frequent intervals.

**Stereotactic Fractionated Radiotherapy (SFR)**

Several published series\textsuperscript{6,35,42,45-48} have described SFR as a primary treatment option for ONSMs. The data from these studies, including visual outcomes, are summarised in Table 1. Summarising the data from all 7 series, the overall disease control in 75 patients was 94.6%. Improvement of visual function occurred within the first 3 months after treatment in 54.7% of the patients. None of the patients had neuroimaging evidence of tumour enlargement during the period of follow-up, and, in fact, a few patients had imaging evidence of a slight decrease in tumour volume. Acute effects of SFR included headache, nausea, local erythema, and focal alopecia. None of these complications were severe or permanent; however, radiation retinopathy was observed in 2 patients 4 years after treatment. The retinopathy was severe in 1 and was associated with vitreous haemorrhage,\textsuperscript{49} whereas the other patient had only retinal microaneurysms.\textsuperscript{42} This latter patient had a large tumour involving the proximal optic nerve adjacent to the globe, and portions of her retina received 54 Gy. Even so, her vision improved from 20/50 and remained stable at 20/25. In a more recent report,\textsuperscript{49} radiation retinopathy occurred 22 months after SFR, resulting in loss of vision from 20/25 to 20/200. The posterior retina in this patient had received 27 Gy to 48 Gy. Other late ophthalmic complications of SFR included cataract in 1 patient, dry eye in 1 and iritis in 2. None of the patients developed radiation optic neuropathy; however, 2 patients continued to lose vision, thought to be from tumour progression.

Late non-ocular side effects reported in these studies included late pituitary dysfunction in 3 patients and radiologically evident cerebral punctate small-vessel fallout in 1. Both are a potential concern after irradiation for posteriorly located ONSMs, particularly those with mild but definite intracranial extension. Interval monitoring of pituitary function in such patients is thus appropriate.

**Surgery**

Extensive removal of ONSMs that extend for some distance within the optic nerve sheath or are located in the posterior orbit and/or optic canal is generally indicated only in rare cases in which there is aggressive tumour growth or disfiguring proptosis. Along with unavoidable and permanent blindness, such procedures may also cause temporary or permanent ophthalmoparesis, ptosis, or both. Unroofing of the optic canal was previously advocated as a method of improving or at least maintaining visual sensory function in patients whose ONSMs were located entirely within the canal;\textsuperscript{26} however, this treatment has been supplanted by radiation therapy (see above), in large part because of the temporary nature of the improvement/ stabilisation with canal unroofing. On the other hand, as noted above, in rare cases of anteriorly located, primarily exophytic tumours with focal involvement of the dural sheath, surgical excision is a potential treatment choice and can be performed without undue risk of iatrogenic visual loss.\textsuperscript{6} Furthermore, optic nerve sheath decompression, with release of trapped cerebrospinal fluid or removal of some tumour followed by radiation therapy, may also be beneficial in cases of acute visual loss.\textsuperscript{50}
Conclusion

The main goals in the management of ONSMs are ensuring a favourable visual outcome, establishing local control of the tumour, and minimising the risks of treatment-related morbidity. Limitations for any treatment study of ONSMs include both the rarity and usually very slow course of the disease, the fact that there often is no tissue diagnosis so that some patients in a treatment trial could have lesions other than an ONSM (e.g., sarcoid of the optic nerve), the necessity of pooling data from multiple different treatment centres, and the need for a long (>10 years) follow-up period to detect late recurrences and late side effects of the treatment.

In the 7 studies described above, the short-term efficacy of SFR in preserving or improving vision appears to be excellent, with more than half of the patients having an improvement within 3 months following treatment. The results also suggest that earlier treatment might offer a better chance of preserving useful vision. Based on the results of published studies as well as our own experience, we believe that SFR is the best option for most cases of progressive or advanced disease. However, because of increasing early diagnosis, more and more patients with presumed ONSMs associated with mild progressive or stable visual loss are being diagnosed, and the decision as to whether to observe or treat is much less clear. We agree with others that longer follow-up to establish the incidence of both lasting results and late toxicity following SFR will be needed to clarify the optimum management of these cases.

Table 1. Summary of Primary Stereotactic Radiotherapy Series

<table>
<thead>
<tr>
<th>Authors (reference number)</th>
<th>Eyes</th>
<th>Period</th>
<th>Mean follow-up</th>
<th>Treatment modality</th>
<th>Treatment regime</th>
<th>Stable</th>
<th>Improved</th>
<th>Worse</th>
<th>Imaging</th>
<th>Complications*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu et al45</td>
<td>5</td>
<td>1994-2001</td>
<td>1-7 years</td>
<td>SFR</td>
<td>25-30 x 1.8</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>Hyperprolactinaemia (2), partial hypophyseal insufficiency (1)</td>
</tr>
<tr>
<td>Pitz et al46</td>
<td>12</td>
<td>1989-2000</td>
<td>37 months</td>
<td>SFR</td>
<td>28 x 1.8</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Narayan et al12</td>
<td>14</td>
<td>1986-2001</td>
<td>51.3months</td>
<td>3D-CFR</td>
<td>28-31 x 1.8</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>Dry eye (1), Iritis (2), Microaneurysms (1)</td>
</tr>
<tr>
<td>Saeed et al6</td>
<td>6</td>
<td>1976-1999</td>
<td></td>
<td>CSFR</td>
<td>0-5</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>Cataract (1)</td>
</tr>
<tr>
<td>Andrews et al17</td>
<td>11†</td>
<td>1996-2001</td>
<td>20.7 months</td>
<td>SFR</td>
<td>28-30 x 1.8</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Baumert et al14</td>
<td>23</td>
<td>1996-2003</td>
<td>20 months</td>
<td>CSFR</td>
<td>25-30 x 1.8-2.0</td>
<td>5</td>
<td>16</td>
<td>2</td>
<td>0</td>
<td>Radiation retinopathy 4 years after treatment (vitreous haemorrhage) (1)</td>
</tr>
<tr>
<td>Richards et al15</td>
<td>4</td>
<td>1999-2002</td>
<td>2 years</td>
<td>SFR</td>
<td>25-27 x 1.7-1.75</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>Radiologically evident cerebral punctate small vessel fall out in the field of irradiation (1)</td>
</tr>
</tbody>
</table>

Eyes The subset of eyes with measurable vision (counting fingers and better)
Delivery strategy FSR: fractionated stereotactic therapy
3D-CFR: 3-dimensional conformal fractionated radiotherapy
CSFR highly conformal stereotactic fractionated radiotherapy
Treatment regime The number of fractions x doses per fraction (Gy)
Stable, improved, worse The treatment effect on visual acuity and visual fields at the last follow up, as defined by author

* Transient complications not listed
† The number of eyes with primary optic nerve sheath meningioma

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