Taking a close look at optic-nerve meningioma

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ABSTRACT

MENINGIOMAS, the most common benign intracranial neoplasms, most often involve the visual pathways in the parasellar and orbital regions, with compression or infiltration of the optic nerves or chiasm. Parasellar tumors may arise anteriorly, from the anterior clinoid, planum sphenoidale, or olfactory groove; posteriorly, from the dorsum or tuberculum sellae; or laterally, along the sphenoid wing. Meningiomas affecting the optic nerve may also arise from the optic canal, and from the optic-nerve sheath itself within the orbit. This review focuses on such primary optic-nerve-sheath tumors.

Keywords: Optic-nerve-sheath meningioma, Optic-nerve tumors, Opticociliary shunt vessels, Optic glioma, Stereotactic radiosurgery, 3D conformal fractionated stereotactic radiotherapy

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CLINICAL PRESENTATION

OPTIC-NERVE-SHEATH meningiomas present most frequently in middle-aged women; 61% of affected patients are female, with a mean age at presentation of 41 years and only 4% under 20 years (age range 2.5-78 years). The tumor typically produces slowly progressive, painless monocular visual loss which is insidious and may proceed undetected until substantial loss has occurred. Bilateral involvement is present at onset in 6%, usually in younger patients. Up to 23% report transient visual loss lasting for several seconds prior to the development of persistent visual loss, presumably due to compromise of the optic-nerve vasculature by tumor compression. Gaze-induced amaurosis occurs rarely due to distortion of the optic-nerve vasculature by the tumor mass in eccentric gaze. Visual loss is usually the only presenting symptom, although fullness and vague discomfort due to orbital congestion may occur; headache is not common. Rarely, facial pain and numbness may be present if the trigeminal nerve is involved. Diplopia may be associated, but usually develops late, with tumors large enough to affect cranial nerves or extraocular muscles at the orbital apex.

Clinical examination reveals a visual-field defect consistent with optic-nerve damage. The most common pattern is diffuse depression with central loss (Figure 1); focal central scotomas and arcuate patterns are less frequent. Rarely, inferior altitudinal loss may result from upward compression of the superior surface of the optic nerve against the falciform ligament at the proximal end of the optic canal. While this pattern of field loss may suggest anterior ischemic optic neuropathy (AION), the usually slowly progressive visual loss and diffuse optic atrophy (as opposed to the acute loss with disc edema seen in AION) should raise suspicion for a compressive lesion at the optic canal. Visual acuity is decreased in 95%, but may not be evident until some time after visual loss. Optic-nerve-sheath tumors, due to their intimate involvement with the nerve, may affect function early, before tumor volume is large enough to produce noticeable proptosis. Ocular motility may be compromised either by direct mechanical involvement of the extraocular muscles by tumor mass, or by involvement of cranial nerves III, IV, or VI at the orbital apex; it is generally a late finding. Eyelid position is most often normal. Ptosis is occasionally present, but retraction is unusual and should prompt consideration of thyroid-related orbitopathy.

The optic disc most commonly is atrophic (49%), but may be edematous (48%), or normal in appearance (3%); atrophy and edema may coexist. Typically, lesions at the orbital apex produce progressive optic atrophy without disc edema, while more anteriorly located tumors result in optic-disc edema early, and may even be associated with central retinal-vein occlusion. Occasionally, the tumor may invade the optic-nerve head itself, with cellular infiltrate visible on the disc surface. Optociliary shunt vessels (retinociliary collateral vessels) are visible on the disc surface in about one third of patients, a reflection of chronic compression and obstruction of central retinal venous outflow; they may be present in atrophic or edematous optic discs (Figure 2). The clinical triad of visual loss, optic atrophy, and optociliary shunt vessels is the classic presentation of optic-nerve-sheath meningioma.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of optic-nerve-sheath meningioma includes inflammatory, ischemic, infiltrative, and compressive etiologies.
The most common inflammatory syndrome, demyelinating optic neuritis, presents with acute or subacute visual loss associated with pain, particularly on eye movement (92% in the Optic Neuritis Treatment Trial).³ Visual loss typically begins to recover in 2 to 3 weeks and most patients regain excellent acuity within 3 to 4 months; gradually progressive painless visual loss (as occurs in optic-nerve meningiomas) is distinctly unusual. Neuroimaging shows enhancement and enlargement of the optic nerve, but the sheath is not preferentially involved, as it is in meningioma (Figure 3).

Atypical optic neuritis, such as that associated with sarcoidosis, vasculitis (lupus), or specific infections (syphilis), may resemble optic-nerve-sheath meningioma in its presentation, with more gradual onset, variable degree of pain, and slower or absent recovery of vision.

Sarcoid optic neuropathy, in particular, may demonstrate clinical and neuroradiologic features that are indistinguishable from meningioma.³ The presence of ocular inflammation such as uveitis and periphlebitis may aid in distinction. Selected patients may require systemic evaluation for granulomatous inflammation.

Orbital inflammatory disease (orbital pseudotumor) may involve the optic nerve; it is almost always painful and usually shows features of external inflammation such as lid edema and conjunctival injection as well as proptosis.³ Neuroimaging usually shows signs of orbital fat and sometimes extraocular muscle involvement with the inflammatory process.

Ischemic optic neuropathy also typically presents acutely, though without pain, and often shows segmental disc edema and altitudinal visual-field loss. It may be progressive initially, but most often stabilizes within 4 to 6 weeks.

Infiltrative and compressive optic neuropathies are more difficult to differentiate clinically from meningioma in that they may also cause gradually progressive visual loss, often with mild proptosis. Neuroimaging, however, provides clear differentiation of these entities. Orbital infiltrative processes such as lymphoma may affect the optic nerve, but usually show more diffuse involvement of the orbital fat and extraocular muscles on neuroimaging. Discrete orbital tumors of any origin may compress the nerve extrinsically but are readily visualized as distinct from the optic-nerve sheath. Disorders producing extraocular muscle enlargement, especially thyroid-related orbitopathy, may result in proptosis and optic-nerve compression. Eyelid retraction and lid lag may be tipoffs to this diagnosis. Sphenoid wing meningiomas, particularly in the medial portion, may present with
frequently associated with anterior (adjacent to the globe) or posterior (orbital apex) focal expansion (Figure 5). The increased size primarily represents thickening of the optic-nerve sheath itself, though the optic-nerve parenchyma may be infiltrated as the tumor grows. Sheath involvement is usually distinguishable from the nerve substance as a bright, enhancing outline surrounding the relatively spared, less bright central nerve substance (so-called “tram-track” appearance on fat-suppressed axial views (Figure 5), allowing differentiation from the diffuse, full-thickness involvement of both nerve and sheath tissue with optic glioma (Figure 4). The type of kinking and buckling of the nerve seen with glioma (Figure 6) is distinctly unusual in meningioma. A focal cystic region

proptosis and gradually progressive optic neuropathy. Finally, primary optic-nerve tumors, most commonly glioma, may masquerade as meningioma (Figure 4). While gliomas usually present in childhood, they may appear in young to middle-aged adults, and often are more aggressive at this age, with progressive visual loss over months. In all these entities, although the clinical presentation may mimic that of optic-nerve meningiomas, the neuroradiologic features of each are characteristic, and aid in diagnosis.

In general, biopsy for tissue diagnosis is unnecessary and may be detrimental. Full thickness biopsy is blinding, and partial thickness or sheath biopsy, which may spare remaining vision, may be misleading, as arachnoidal proliferation surrounding an optic-nerve glioma may be misdiagnosed as meningioma. In general, tissue biopsy is reserved for atypical cases in which an alternate diagnosis, such as malignant glioma or sarcoid optic-nerve infiltration, is suspected on the basis of unusually rapid progression or atypical associated findings such as ocular inflammation. Neuroimaging is sufficient for diagnosis in most cases.5

NEURORADIOLOGIC FEATURES

Optic-nerve-sheath meningiomas have a distinctive radiologic appearance usually sufficient for specific diagnosis; however, routine brain images, whether computed tomography (CT) or magnetic resonance imaging (MRI), are inadequate to visualize the details of the optic nerve along its entire course. MRI of the parasellar region, with thin-section (1.5 mm) orbit views, utilizing fat-suppression technique and gadolinium administration, is essential for this purpose. Meningiomas typically demonstrate tubular, diffuse enlargement of the overall diameter of the optic-nerve sheath/nerve complex, frequently associated with anterior (adjacent to the globe) or posterior (orbital apex) focal expansion (Figure 5). The increased size primarily represents thickening of the optic-nerve sheath itself, though the optic-nerve parenchyma may be infiltrated as the tumor grows. Sheath involvement is usually distinguishable from the nerve substance as a bright, enhancing outline surrounding the relatively spared, less bright central nerve substance (so-called “tram-track” appearance on fat-suppressed axial views (Figure 5), allowing differentiation from the diffuse, full-thickness involvement of both nerve and sheath tissue with optic glioma (Figure 4). The type of kinking and buckling of the nerve seen with glioma (Figure 6) is distinctly unusual in meningioma. A focal cystic region
(perioptic cyst) may be present, often near the globe and surrounding the nerve substance, representing a collection of CSF presumably trapped by tumor obstruction of flow within the sheaths. This cystic component differs from the cystic spaces within gliomas, which are the result of mucinous degeneration within the nerve substance itself (Figure 6). In more aggressive meningiomas, extradural extension may produce an irregular, sometimes fluffy, margin representing breakthrough into the adjacent orbital fat. Meningiomas tend to be isointense or slightly hyperintense relative to brain on both CT and MRI (T1 and T2), and enhance prominently with contrast. This is another point of distinction from gliomas, which may be hyperintense on T2, and in some cases do not enhance as brightly with contrast. The pattern of intracranial extension of meningioma also differs from that of glioma. Meningioma extension proceeds along the dura of the optic canal and onto the planum sphenoidale, often anterior to the optic nerve and chiasm. There may be localized nodular expansion of tumor, which extends superiorly into brain substance and away from the nerve itself. Glioma, on the other hand, extends intrinsically within the nerve substance, expanding it along its course, which may include the chiasm and optic tract.

Several features are best demonstrated on CT: up to 50% of meningiomas may show calcification within their substance, with an encircling band around the affected portion of the nerve (noncontrast views are necessary to visualize this pattern); adjacent bone, particularly the optic canal or anterior clinoid process, may show hyperostosis; and finally, in rare cases, pneumosinus dilatans, a condition in which enlarged, air-filled posterior ethmoid and sphenoid sinuses adjacent to tumor may be the first sign of a meningioma, when the intracanalicular tumor is still too small for detection.

**HISTOPATHOLOGY**

Meningiomas of the optic-nerve sheath are thought to arise from meningothelial “cap cells” lining the arachnoid villi of the intracanalicular and intraorbital optic-nerve meninges. They tend to assume either (a) the meningothelial, or syncytial, pattern of sheets of polygonal cells with interspersed vascular trabeculae, or (b) the transitional pattern, in which spindle or oval cells are arranged in whorls and psammoma bodies are more common. Angioblastic and fibroblastic forms are usually seen only in primary intracranial tumors. The tumors proliferate within the subarachnoid space, often infiltrate the optic-nerve substance along pial septae and perivascular spaces, and may invade and extend through the dura into surrounding orbital tissues. They may invade bone, inciting hyperostosis and bony proliferation. They may extend intracranially to the chiasm and across the planum sphenoidale to the contralateral optic nerve, but they do not tend to invade other brain structures. Tumors may arise at multiple sites simultaneously, and thus it may be difficult to assess whether large areas of involvement result from spread from a single lesion or multiple separate origins. Growth of the tumor compresses optic-nerve axons, with resultant direct damage, as well as secondary ischemic damage due to obliteration of the pial vascular supply.

**NATURAL HISTORY**

Untreated, optic-nerve-sheath meningiomas generally grow slowly, with gradually progressive loss of vision in the affected eye over years, estimated in one series at 1 to 3 Snellen lines acuity loss per year.2 The tumors do not metastasize and only rarely invade the brain parenchyma; the mortality rate is essentially nil.9 The primary risk related to growth is that of visual loss, either in the affected or the contralateral eye, the latter via spread along the planum sphenoidale. There have been no reported cases of spread to the contralateral optic nerve from tumor that presented initially with involvement limited to one orbit.10 Canalicular tumors, however, show a higher rate of bilaterality. Approximately 15% of these cases demonstrate extension of the tumor intracranially at presentation, and the risk of growth to involve the contralateral nerve in this instance is estimated at 2 to 4%.11

Alper11and Wright, et al.12 have both proposed that optic-nerve-sheath meningiomas in children tend to be more aggressive, with higher recurrence and mortality rates. Alper reported that 4 of 15 cases died with intracranial extension on follow-up. However, Dutton reported that deaths in this series resulted from operative complications and late-onset secondary intracranial tumors—not the original tumors—suggesting that the evidence for more aggressive course in children was inconclusive.1 Nevertheless, more careful observation of children for evidence of rapid growth seems appropriate. Additionally, investigation for evidence of neurofibromatosis (NF) in children presenting with sheath meningioma is indicated. As with optic gliomas (29%), the incidence of NF in cases of meningioma (12%) is higher than in the general population (0.05%).13 Conversely, 15% of NF patients are estimated to develop optic glioma;4 development of optic-nerve meningioma is less common, though precise figures are not available. The influence of associated NF on clinical course of optic-nerve meningioma is uncertain.

**TREATMENT**

Treatment options have included observation, surgical excision of sheath tumor, surgical excision of sheath tumor and optic nerve, optic-nerve-sheath decompression, optic-canal decompression, hormonal therapy, standard
(fractionated) external beam radiotherapy, stereotactic (gamma knife, nonfractionated) radiosurgery, and more recently, 3D conformal stereotactic (fractionated) radiotherapy. Surgical excision of tumor alone (preserving optic-nerve tissue) has been attempted in anteriorly located extrinsic tumors, with occasional initial benefit, but in general, stripping of tumor from the optic nerve carries a high risk of sacrificing the pial circulation to the nerve, with loss of vision and incomplete tumor removal. Optic-nerve-sheath decompression has been attempted in order to delay visual loss by reducing perineural pressure, but the procedure provides egress for tumor cells, and intraorbital spread and recurrence have been associated with this approach. Optic-canal decompression has been proposed for certain intracanalicular tumors, again in an attempt to temporize and maintain vision by reducing compression without tumor removal. Very little long-term follow-up data are available for either of these approaches. Hormonal therapy has also been attempted based on initial observations that meningioma growth was related to menstrual cycle and pregnancy, and later laboratory evidence that meningioma cell growth could be inhibited by both progesterone (mifepristone) and estrogen (meptitostane) antagonists. Mifepristone (RU-486) has been the most extensively studied, primarily in unresectable central-nervous-system (CNS) meningiomas, but there are little data for effectiveness.

Surgical therapy of optic-nerve-sheath meningioma, with excision of tumor and optic nerve en bloc, has been the primary method of intervention to prevent spread to the contralateral optic nerve or chiasm. There is no benefit to the affected eye, as therapy is blinding; there is generally no benefit to overall neurologic status and survival, as there is virtually no risk of other CNS or systemic involvement from the tumor. Surgical intervention typically is only considered in the face of progressive visual loss, but the timing of intervention remains controversial. Some authors advocate early surgery if the tumor is limited to the orbit, particularly anteriorly, as this situation affords the best opportunity for complete resection, possibly without the need for an intracranial approach. Others propose observation in this situation, as there is essentially no risk of extension to the contralateral nerve, and surgery may be avoided entirely if the tumor is found to be indolent. The value of this approach is underscored by a report of Arnold et al., demonstrating histopathologic evidence of meningioma cells at the chiasm in a case in which meningioma appeared on neuroimaging to be limited to the orbit, and which was nonprogressive over years; a surgical approach was unnecessary in the face of clinical stability and would have been ineffective to eliminate meningioma cells regardless. Many authors suggest surgical excision for tumors presenting with intracranial extension, but in the face of a small, stable tumor, which is not threatening the contralateral optic nerve, we typically recommend observation only.

Radiation therapy (standard external beam irradiation) of optic-nerve-sheath meningiomas was proposed by Smith in 1981 and was reported in isolated cases subsequently through 1992, with 9 of 12 cases showing visual improvement, in some cases dramatically [from hand movement (HM) to 20/70 in Smith’s case, from counting fingers (CF) to 20/60 in another]. The proximity of the sheath to intact optic-nerve tissue and in some cases the infiltration of tumor into the nerve substance, however, creates risk of radiation necrosis of the nerve, although meaningful data on complication rates are lacking due to small numbers and limited follow-up. The development of stereotactic techniques has enabled better localization of radiation dose and sparing of surrounding tissues. Stereotactic radiosurgery (gamma knife) has been utilized with substantial benefit in CNS tumors, but the very high dose of radiation administered over a short time period potentially increases the risk of optic-nerve radionecrosis. Optic neuropathy has been reported in roughly 10% of cavernous sinus meningiomas treated by this technique. Although a recent study by Stafford et al. reported an incidence of 2% for parasellar tumors, the risk for primary optic-nerve-sheath meningiomas, in which the tumor is intimately involved with the optic nerve, is felt to be substantially higher; this modality is not frequently utilized for sheath tumors.

In recent years, 3D conformal stereotactic radiotherapy has become the first option for cases requiring therapy. This technique, using fractionated rather than single-dose stereotactic techniques and intensity modulation to limit dose to surrounding tissue, has substantially improved therapeutic results. Multiple reports document visual improvement in cases with previously progressive visual loss, and radionecrosis has been a rare occurrence even with prolonged follow-up. In cases with useful but deteriorating vision or in which there is neuroimaging evidence of tumor growth toward the contralateral optic nerve, this is currently the preferred treatment. The decision whether to treat cases presenting initially with minimal or no intracranial spread and without progressive visual loss remains controversial.

A recent large-scale multicenter study by Turbin et al. retrospectively reviewed the visual outcome and complication rates for various therapeutic options, including observation, surgery only, radiotherapy only, and surgery with radiotherapy. The series predated the development of the 3D conformal stereotactic technique. Patients receiving radiotherapy only demonstrated a significantly better visual acuity at follow-up than all other groups, with lower complication rate than cases that included surgical
therapy. While the study had limitations, it confirmed the recommendation that fractionated radiotherapy be considered as initial therapy in patients with useful vision.

**MANAGEMENT GUIDELINES**

Management of optic-nerve-sheath meningiomas requires consideration of the patient’s age, visual function, degree of tumor extension, and the demonstrated clinical and radiologic course (aggressive growth versus stability). Clinical examinations with visual acuity, visual field, and fundus evaluations at three- to six-month intervals are recommended during the first 1 to 2 years, increasing the interval to yearly if examinations are stable. MRI of the brain with orbit-specific views using fat-suppression technique and contrast administration is repeated at 6 months, then yearly if stable.

**Tumor limited to orbit**

If useful vision is present and tumor is stable, observation alone is the usual first option. We currently reserve therapy for evidence of severe initial visual loss, progressive visual loss, or tumor extension toward the contralateral optic nerve on neuroimaging. If no useful vision remains, surgical excision has been the standard of care, although with the advent of 3D conformal stereotactic radiation, consideration is now given to this modality to prevent progression without the need for surgical intervention, particularly in view of the lack of evidence of reported spread to the contralateral optic nerve in these cases.

**Tumor with intracranial extension**

Surgical excision has been proposed in the past for all cases with intracranial extension, but more conservative approaches are now more common. If useful vision is present, intracranial extension is limited (not encroaching on the planum sphenoidale), and tumor is stable, observation alone is an option, although with the advent of 3D conformal stereotactic radiation, we advocate its early use in this situation. It is certainly indicated if there is evidence of progressive visual loss or neuroimaging evidence of growth. With poor vision and intracranial extension with growth, most experts recommend surgical excision.

For any case, intraorbital or intracranial, in which preservation of vision is possible, the use of 3D conformal stereotactic radiation must be considered as a primary therapy; however, in all such cases, regardless of visual level or clinical course, therapy must be selected on an individual basis. In all cases, age and general health of the patient must be considered. Elderly or otherwise frail patients may be poor surgical risks and more likely to be candidates for radiation or for observation only, while children, in which the long-term risk for development of secondary malignancies with radiation therapy is greater, may be more likely candidates for surgery. Finally, surgical excision in cases with poor vision may be considered for disfiguring proptosis or intractable pain.

**References**