

Radiotherapy for Meningiomas of the Anterior Visual Pathway

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Radiation Therapy for Meningiomas of the Anterior Visual Pathway

- Definitions
- Clinical presentations
- Management options
- Radiation therapy options and results
- Recommendations

Secondary Meningioma Involving the Anterior Visual Pathway

Cavernous sinus

Tuberculum sellae

Anterior clinoid

Sphenoid wing

“Primary” Meningiomas Involving the Anterior Visual Pathway: Primary ONSMs)

Clinical Manifestations

Depend on Location

- Anterior (usually primary ONSMs)
- Posterior (retrobulbar) (may be primary ONSMs or secondary)

Anterior Presentation

- Variable loss of acuity, color vision, and field
- Relative afferent pupillary defect (not always)
- Proptosis (very mild when present)
- Swelling of optic disc (usually no hemorrhages or exudates)
- Retino-choroidal collaterals
 - With visual loss and optic atrophy or chronic swelling
 - Usually a late finding

Posterior (Retrobulbar) Presentation

- Progressive unilateral or bilateral visual loss
- Evidence of unilateral or bilateral optic neuropathy
- Normal or pale optic disc(s)

Management Options

- Observation appropriate if:
 - Secondary meningioma
 - No significant visual dysfunction
 - Patient has major medical issues
 - Primary ONSM with:
 - No significant visual dysfunction
 - No significant progression of visual loss
 - No significant intracranial extension
- No medical therapy beneficial
 - Antiprogestosterone or antiestrogen agents work in vitro but of no major clinical benefit
 - Hydroxyurea tried without success
 - Oncolytic virus?
- Surgery
 - Alone or combined with radiotherapy for TS/AC/SR meningiomas
 - Combined with radiotherapy for CS meningiomas
 - For primary ONSMs that appear as paraneural mass (S Pitz et al.)

 - ONS fenestration in combination with radiotherapy for primary ONSM (R Turbin et al.)

Radiation Therapy for Meningiomas Involving the Anterior Visual Pathways:

The Beginning

- There is no question that visual palliation can be achieved [with radiation therapy] in some cases of optic nerve sheath meningioma.
 - JL Smith et al. J Clin Neuroophthalmol 1:85, 1981
- Irradiation in the range of 5,000 to 5,500 cGy is effective either alone or in combination with surgical excision in stabilizing or improving vision in anterior visual pathway meningiomas.
 - ML Kupersmith et al. Ann Neurol 21:131, 1987

Radiation Therapy: The Problem

- How do you provide sufficient radiation to destroy or stabilize the tumor and improve or stabilize vision without harming adjacent tissue?

<u>Organ at risk</u>	<u>Tolerance (Dmax)</u>
• Brainstem	<52 Gy
• Optic nerve/chiasm/tract	<52 Gy
• Brain	<66 Gy
• Eye/retina	<45 Gy
• Lacrimal gland	<30 Gy
• Hypothalamic/pituitary axis	<45 Gy

Radiation Therapy Options

- Conventional fractionated radiation therapy--most used in past
- Stereotactic radiosurgery--insufficient experience
- Stereotactic (3D conformal, IMRT) fractionated radiation therapy--current treatment of choice for both primary and secondary tumors
- Proton beam therapy

Conventional Fractionated Radiation Therapy

- Usually consists of about 54 Gy given in 1.8-2.0 Gy daily fractions
- Can be performed by almost any radiation center
- May be associated with loss of vision from radiation retinopathy or optic neuropathy

Conventional Fractionated Radiation Therapy for Secondary Meningiomas

H Dufour et al. Neurosurgery 48:285, 2001

- 31 patients separated into two groups
 - Group I: 17 pts treated with surgery + RT
 - Group II: 14 pts treated with RT alone
- F/u period ranged from 2 to 16 years (median, 6.1 yrs)
- No permanent complications from RT
- 30% complained of transient tinnitus, dizziness, headaches, or general weakness
- **Visual Outcome (%): Excellent with 71% improved or normal**

Conventional Fractionated Radiation Therapy for Primary ONSMs

- RE Turbin et al. (Ophthalmology 109:90, 2002)
 - 64 patients with ONSMs
 - Patients managed with observation, surgery, radiation therapy (most with conventional fractionated), or combination of surgery followed by radiotherapy
 - ≥ 50 months follow-up
 - Range, 51-516 months
 - Mean, 150 months
- Visual acuity measures at baseline same among all four groups
- Patients who were followed without intervention, operated, or who had surgery followed by radiation therapy all experienced a significant decline in vision over time
- Only patients treated with radiation therapy alone significantly improved or at least had stable vision compared with pretreatment values
- Complications in 33% (dry eyes, retinopathy, cataract)

Conventional Fractionated Radiation Therapy for Primary ONSMs

- 22 patients with presumed ONSM
- Ave dose: 54 Gy
- Follow-up: 51-156 months (mean: 55 mo)
- 9 improved, 11 stable, 2 worsened
- Complications in 6/22 (27%): dry eyes, cataract, radiation retinopathy

P Saeed et al. Br J Ophthalmol 94:564, 2010

Stereotactic Radiosurgery

- Requires Gamma Knife, LINAC, or Cyberknife
- Need thermoplastic mask and stereotactic frame (not needed with Cyberknife)
- Radiation delivered by multiple arcs
- Total dose given: 1200-3600 cGy in 1-5 fractions

Stereotactic Radiosurgery for Secondary Meningiomas

JR Adler Jr et al. Neurosurgery 59:244, 2006

- 27 pts
- Rx with 2-5 sessions
- Ave total dose: 20.3 Gy
- F/U: 6-96 mo (mean: 49 mo)
- Improvement or stabilization of visual function in 94%

Stereotactic Radiosurgery for Secondary Meningiomas

JC Ganz et al. Br J Neurosurg 24:233, 2010

- 67 patients
- Maximum dose 8-10 Gy
- Minimum f/u of 25 mo
- Improvement in 21 pts (38.7%)
- No patient experienced worsening of vision

Stereotactic Radiosurgery for Primary ONSMs

- One patient reported by Y Kwon et al. J NS (Suppl) 102:143-146, 2005
 - 44F whose vision improved from 20/200 pretreatment to 20/15 over 7 months
- Too soon to tell if this technique is appropriate for patients with good visual function, but...

Stereotactic Radiosurgery for Meningiomas of the Anterior Visual Pathway

- Safe
 - No mortality
 - Minor and generally transient morbidity
- May result in improved visual function
- Usually results in stable or reduced tumor volume
- No long-term studies

Stereotactic (3D Conformal vs Intensity-Modulated) Fractionated Radiation Therapy

- Both provide focused photon radiation that conforms to the size and shape of the lesion
- IMRT uses intensity-modulated beams delivered with dynamic multileaf collimators to vary the dosage (intensity) **within a single beam**
- May use stationary or helical gantry
- Head immobilized during treatment sessions but stereotactic frame not required
- Tumor receives about 50 Gy in 1.8-2.0 Gy fractions

SFR for Secondary Meningiomas Involving the Anterior Visual Pathway

- Generally good tumor control
- Side effects rare and mild
- Visual damage rare short-term and long-term
 - 27 pts with skull base meningiomas
 - Most involved anterior visual pathway
 - 2-year follow-up
 - No visual loss in any patient

G Minniti, R Muni. Rivist Med 14(Suppl 3):175-177, 2008

Long-Term Visual Results with SFR for Secondary Meningiomas

- 186 pts with TS/CS/SR meningiomas (317 total)
 - Median dose 57.6 Gy (1.8 Gy fractions)
 - F/U: 1.2-14.3 yrs (median, 5.7 yrs)
 - 140 pts with decreased vision before rx
 - 3 returned to normal
 - 7 improved
 - 120 unchanged
 - 10 worsened
- S Milker-Zabel et al. Int J Radiol Biol Phys 61:809, 2005

SFR for Primary ONSMs

- Short-term results of treatment promising
 - JK Liu et al. Neurosurgery 50:950, 2002
 - DW Andrews et al. Neurosurgery 51:890, 2002
 - S Pitz et al. Br J Ophthalmol 86:1265, 2002
 - G Becker et al. Int J Radiat Oncol Biol Phys 54:1422, 2002
 - S Narayan et al. Int J Radiat Oncol Biol Phys 56:537, 2003
 - M Landert et al. J Neuroophthalmol 25:86, 2005
 - S Milker-Zabel et al. J Neurooncol 94:419, 2009
- Long-term results also positive
 - RL Lesser et al. Br J Ophthalmol 2009 Dec 3 [Epub before print] (Br J Ophthalmol 94:561, 2010)
 - P Metellus et al. Int J Radiat Oncol Biol Phys 2010 (Epub before print)
 - P Saeed et al. Br J Ophthalmol 94:564, 2010

Long-Term Results after SFR for ONSMs

- 20 patients followed at least 5 years (61-156 mo)
- Mean f/u: 89.6 (RLS); 98 months (PM)
- Median f/u: 73 months (RLS); 90 months (PM)
- 18 pts with vision at time of SFR: All but one improved or remained stable
- 1 pt developed radiation retinopathy 2 yrs after SFR; 1 pt had bilateral dry eyes
- No patient experienced growth of lesion

Long-Term Results after SFR for ONSM

- 12 pts followed for at least 51 months
 - Range: 51-156 months
 - Mean: 58.32 months
- Improved 5, stable 6, worsened 1
- Complications: dry eyes, cataracts, radiation retinopathy
 - No difference from conventional fractionated radiation results
 - P Saeed et al. Br J Ophthalmol 94:564, 2010

Proton Beam Therapy for Meningiomas Involving the Anterior Visual Pathway

- Requires cyclotron
- As of April 2010, there were a total of 29 proton therapy centers in Canada, China, England, France, Germany, Italy, Japan, Korea, Russia, South Africa, Sweden, Switzerland, and USA
- Theoretically allows more precise focusing than FSR
- Few reports; no long-term f/u

Summary

1. It's ok to observe patients with meningiomas that affect the anterior visual pathway, particularly ONSMs
 - a. Clinical assessment and MRI at regular intervals
 - b. Patient must be told to contact physician if any deterioration of vision.
2. Conventional fractionated radiation therapy can be used, either alone or in combination with surgery for TS, SR, CS and AC meningiomas with reasonable safety and efficacy
3. The efficacy of stereotactic radiossurgery for both secondary and especially primary meningiomas is unclear (small numbers, short-term data only).
4. Stereotactic fractionated radiotherapy (IMRT) is reasonable for most patients with secondary meningiomas and is the current standard of care for most patients with ONSMs who require treatment
 - Many patients improve, often dramatically, but visual complications may still occur
 - Perhaps lower dose would be just as effective and associated with fewer complications
 - May be given at any level of visual function
 - Both short-term and long-term data very positive
5. Proton beam therapy may offer some benefit over therapy with photons (SR, FSR) but no long-term data available.

Conclusion

There have been many advances in the treatment of both secondary and primary meningiomas that involve the anterior visual pathway within the past several years with respect to radiation therapy, with more (hopefully) to come in the future!