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Outcomes of Cataract Surgery Following Radiation Treatment for Retinoblastoma

John F. Payne, MD, Amy K. Hutchinson, MD, G. Baker Hubbard III, MD, and Scott R. Lambert, MD

Departments of Pediatric Ophthalmology and Vitreoretinal Surgery and Disease, Emory Eye Center, Emory University, Atlanta, GA

Abstract

Purpose—To report the outcomes after cataract extraction in eyes previously treated for retinoblastoma.

Methods—We reviewed the medical records of consecutive patients treated with cataract extraction at our institution for radiation-induced cataract following retinoblastoma treatment between 1992 and 2007.

Results—Twelve eyes of 11 patients were included. The median age at diagnosis of retinoblastoma was 7.4 months. The median quiescent interval before cataract surgery was 34.6 months (range: 17 - 240 months). All patients underwent limbal-based extracapsular cataract extraction with scleral-tunnel wound construction. Anterior vitrectomy and posterior capsulotomy were performed in seven eyes; an intraocular lens was placed in 10 eyes. A laser capsulotomy was subsequently performed in five eyes. No postoperative complications occurred. One patient underwent a vitrectomy for vitreous hemorrhage five years after cataract extraction. The median follow-up after surgery was 6.01 years (range: 1.1 - 12.3 years). Final visual acuity was between 20/20 and 20/60 in six eyes, between 20/70 and 20/200 in two eyes, and worse than 20/200 in four eyes. Every patient with documented preoperative vision (10 eyes) had improved vision at final examination. No intraocular recurrences or metastases occurred. Two patients developed secondary rhabdomyosarcomas, one of whom succumbed to their disease.

Conclusions—Limbal-based cataract extraction in our series was not associated with tumor recurrence or metastasis. The optimal quiescent interval is not known, however, no tumor recurrences occurred in our series when a minimum 17 month quiescent period was achieved. Visual improvement was noted in every patient, although several patients only experienced modest gains.

Introduction

Recent advances in the diagnosis and treatment of retinoblastoma have been considerable. Enucleation has been replaced by globe-conserving therapy in many cases.¹ External beam radiotherapy was the treatment of choice as primary therapy for intraocular retinoblastoma for much of the 20th century.² During the early 1990's chemotherapy replaced external beam radiotherapy as the most commonly used primary treatment for intraocular retinoblastoma.² Chemoreduction has been used with cryotherapy and laser thermal therapy to avoid the side effects of external beam radiotherapy, which include cataract, retinopathy, orbital

Corresponding author and reprint requests to: Amy K. Hutchinson, MD, Emory Eye Center, 1365 B Clifton Road, Suite B4514, Atlanta, GA 30322, Phone: (404) 778-5292, Fax: (404) 778-5128, ahutch2@emory.edu.

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hypoplasia, and secondary tumors.²⁻⁸ External beam radiotherapy continues to be used as salvage therapy for those tumors that do not adequately respond to chemotherapy and other treatments.⁹

One of the most common ocular complications of external beam radiotherapy for retinoblastoma is cataract formation, which typically occurs one to three years following treatment.^{10,11} Several studies have shown that cataract extraction with and without intraocular lens (IOL) placement in patients who have previously received radiation for retinoblastoma treatment is generally not associated with tumor recurrence or spread.^{9,11-19} The purposes of this study were to assess the visual outcomes, complications, and tumor recurrences in patients at our institution who have undergone cataract surgery for radiation-induced cataracts following treatment for retinoblastoma, and to review the literature.

Patients and Methods

The Institutional Review Board of the Emory University School of Medicine approved this study. We reviewed the medical records of consecutive patients with a diagnosis of retinoblastoma, who subsequently underwent cataract extraction at Emory Eye Center between January 1, 1992 and December 31, 2007. All patients had previously received radiation therapy, either external beam radiotherapy or ¹²⁵I plaque brachytherapy, to treat their retinoblastoma. A total of 12 eyes from 11 patients were included for analysis. Ten eyes received external beam radiotherapy only, one eye received ¹²⁵I plaque brachytherapy only, and one eye received both external beam radiotherapy and ¹²⁵I plaque brachytherapy. The decision to perform cataract surgery was considered carefully and based on a decline in visual acuity resulting from a lenticular opacity as determined by potential acuity testing, glare testing, and clinical examination, or a combination thereof. Seven patients were monocular at the time the decision to operate was made. All patients had been deemed quiescent for a sufficient time period, usually greater than 18 months, before cataract surgery was undertaken.

Data collected included demographic information, age at diagnosis of retinoblastoma, stage at worst presentation (both Reese-Ellsworth and International Classification), and location of the tumors. The retinoblastoma treatment modalities used, and the interval between diagnosis and cataract extraction were recorded, as was the preoperative and postoperative visual acuity, length of follow-up, and intraoperative and postoperative complications. Snellen visual acuity was used when possible. Allen pictures were used in younger children in whom Snellen acuities could not be determined. All attempts were made to use linear optotypes, so as to not underestimate amblyopia. If linear acuity was not possible, isolated optotypes with crowding bars was attempted. Any intraocular retinoblastoma recurrence or metastasis was also noted, as was the occurrence of secondary tumors.

Surgical Technique

A complete examination under anesthesia was performed in all patients just prior to cataract extraction. The examination included keratometry and axial length measurements, retinoscopy, and dilated funduscopy. All axial length measurements were made using immersion biometry. Five eyes underwent extracapsular extraction, IOL implantation, posterior capsulotomy, and anterior vitrectomy. Five additional eyes underwent extracapsular cataract extraction with IOL implantation without primary posterior capsulotomy or anterior vitrectomy. The decision to perform a posterior capsulotomy and anterior vitrectomy was made intraoperatively and based on the patient's age and the clarity of the visual axis after the cataract had been aspirated. Younger patients and those with posterior capsule opacification usually received primary capsulotomy and anterior

vitrectomy. When an IOL was used (10 eyes), it was successfully implanted into the capsular bag in all cases. In two eyes, extracapsular cataract extraction was performed in conjunction with a posterior capsulotomy and anterior vitrectomy without IOL implantation (patients 2 and 5). These two were the earliest patients in this series, and had surgery in 1992 and 1995, respectively. They were left aphakic based on the surgeon's preference at that time. A limbal-based approach, where a scleral-tunnel wound and paracentesis are created, was used in all cases. The wound and paracentesis were sutured close at the conclusion of the surgery in all cases. A medial rectus resection and lateral rectus recession was also performed on the involved eye in one patient just prior to cataract extraction (patient 7). A subconjunctival injection of dexamethasone and cefazolin was performed at the end of each procedure unless the patient was allergic to penicillin, in which case, only dexamethasone was injected.

After surgery, patients were instructed to use antibiotic drops for at least one week and topical prednisolone acetate 1% for at least one month. Amblyopia was treated with patching as needed.

Results

The patient demographics and relevant clinical information for the 12 eyes included in this study are shown in E-Supplement 1, which can be found at www.jaapos.org. Patient 1 had bilateral sequential cataract extractions, whereas all other patients had unilateral surgery. Ten of the 11 patients had bilateral tumor involvement and seven of these patients required enucleation of the more involved eye.

The median age at retinoblastoma diagnosis was 7.4 months (range: 9 days to 2.8 years) and the median age at cataract surgery was 4.4 years (range: 2.7 to 20.9 years). The median quiescent interval, which was considered to be the interval between the date of last retinoblastoma treatment and the date of cataract surgery, was 34.6 months (range: 17 months to 20.0 years). Preoperative visual acuity ranged from 20/70 to light perception. Two patients (1 and 5) were untestable with Allen pictures or Snellen acuity prior to surgery. No intraoperative or postoperative complications were encountered. All five eyes in which the posterior capsule was left intact at the time of surgery, subsequently required a neodymium-yttrium-aluminum-garnet (Nd:YAG) laser capsulotomy. Three other patients also required Nd:YAG laser treatment after surgery for capsular or hyaloidal fibrosis, in spite of having a primary posterior capsulotomy and anterior vitrectomy. The median interval between cataract extraction and YAG capsulotomy was 4 months (range: 1 to 43 months). The median follow-up for the five patients who subsequently underwent Nd:YAG capsulotomy was 20 months (range: 7 to 72 months).

Overall, the median follow-up after cataract surgery was 6.01 years (range: 1.1 to 12.3 years). Final visual acuity was between 20/20 and 20/60 in six eyes, between 2/70 and 20/200 in two eyes, and worse than 20/200 in four eyes. Table 1 displays the preoperative and postoperative visual acuities as well as the length of follow-up for the patients in this study. All patients with documented preoperative visual acuity (10 eyes) had improved vision at the final follow-up examination. No intraocular recurrence, extraocular extension or metastasis was noted at the final follow-up examination in any patient. Amblyopia was considered to be a cause of postoperative vision limitation in two of the 12 eyes and macular scarring was felt to be the cause of postoperative vision limitation in three eyes. Complications of radiation, such as keratopathy, retinopathy, or optic neuropathy, were a cause of final vision limitation in six eyes.

Patient 10 developed severe radiation retinopathy with neovascularization and vitreous hemorrhage seven years after external beam radiotherapy (four years after cataract extraction). Because of the severe proliferative retinopathy, this patient underwent an injection of bevacizumab 59 months after cataract extraction. Six weeks after this injection, a pars plana vitrectomy was performed in conjunction with epiretinal membrane peeling, air-fluid exchange, and endolaser treatment. Six months after this procedure the patient developed recurrent vitreous hemorrhage and underwent a repeat bevacizumab injection. No intraocular recurrence has been noted eight months after the pars plana vitrectomy, but the vision continues to be limited by vitreous hemorrhage and proliferative radiation retinopathy.

Two patients developed secondary rhabdomyosarcomas (1 and 2). Patient 1 developed an orbital rhabdomyosarcoma 12 years after the cataract extraction in his right eye. This patient is alive three years after repeat orbital radiation, although he has developed severe radiation keratopathy in the right eye. Patient 2 developed facial swelling two months after cataract extraction, and was diagnosed with a stage IV embryonal rhabdomyosarcoma. This patient subsequently died as a result of her secondary tumor 15 months after diagnosis.

Discussion

The purpose of this study was to assess the outcomes of patients who underwent cataract extraction for radiation-induced cataracts following retinoblastoma treatment. We found that cataract extraction via a limbal approach was not associated with retinoblastoma recurrence or metastasis after a mean follow-up of six years. Visual acuity improved after cataract extraction in all patients in our series, although four patients had counting fingers vision or worse at last follow-up.

Intraocular surgery after treatment for retinoblastoma poses unique challenges. Of particular concern is the risk of dissemination of tumor cells at the time of surgery. Table 2 summarizes the results of 128 eyes that have undergone cataract extraction for radiation-induced cataract following retinoblastoma over the past 22 years. There were only 9 cases of retinoblastoma recurrence and no cases of systemic metastasis among them. Brooks et al reported 3 cases of tumor recurrence.¹³ In each of these eyes, surgery was approached via a pars plana or pars plicata incision, and all 3 eyes had anterior tumors and vitreous seeding prior to external beam radiotherapy with persistent vitreous haze present at the time of cataract surgery. Honavar et al reported 5 cases of recurrence after cataract surgery.¹⁸ The authors did not find any specific predisposing factors for tumor recurrence. However, when looking at all of their patients in this series, including anterior segment and posterior segment surgeries, the patients with a favorable outcome (26 eyes) had a median quiescent interval of 26 months, whereas the patients with an unfavorable outcome (19 eyes) had a median quiescent interval of 6 months. An unfavorable outcome was defined as the presence of tumor recurrence, need for enucleation, or systemic metastasis. Moshfeghi reported one case of retinoblastoma recurrence after cataract surgery, ultimately requiring enucleation.¹⁹ While no predisposing factors were identified in this patient, it was noted that the quiescent interval was only 12 months prior to cataract surgery. Adequate tumor treatment and a sufficient quiescent interval appear to be critical in preventing tumor recurrence and metastasis. While the optimal quiescent interval is not known, the two most recent reports by Portellos¹¹ and Miller⁹, as well as this series, have shown no tumor recurrences when the quiescent interval was at least 16 months.

A summary of the literature of eyes that have undergone pars plana vitrectomy and scleral buckling procedures are shown in E-supplements 2 and 3, respectively. These tables can be found at www.jaapos.org. The risk of tumor recurrence and metastasis appears to be higher

in this group of patients who have undergone posterior segment surgeries, with 16 total cases of tumor recurrence and 3 cases of metastasis. Honovar and colleagues reported the largest series, and they suspected that eyes that required a scleral buckling procedure or pars plana vitrectomy were more likely to have advanced retinoblastoma, and therefore, a higher risk of recurrence.¹⁸ Moshfeghi and colleagues concluded that rhegmatogenous retinal detachments are an ominous sign for both visual acuity and eye salvage.¹⁹ They hypothesized that tumor reactivation could place mechanical stress on the retina, resulting in stretching of an already damaged tissue and thus allowing microscopic breaks to form. Because eyes that require posterior segment surgery may be associated with a higher risk of tumor reactivation, these surgeries should be considered with caution and proper counseling should take place when obtaining informed consent.

Controversies in pediatric cataract management include the surgical approach, and the management of the posterior capsule and anterior vitreous. In the setting of prior treatment for retinoblastoma, these decisions take on even greater importance with the added concern for reactivation or metastasis of the tumor(s). Both clear-corneal and pars plana approaches have been used with success in children undergoing cataract surgery after treatment for retinoblastoma. Although Brooks et al advised against pars plana incisions based on their experience of tumor recurrence, other series have not reported tumor recurrence with a pars plana approach. Miller and associates reported a series of 16 eyes, all of which underwent a pars plana vitrectomy in addition to cataract extraction, and showed no evidence of tumor recurrence in their series.⁹ Although we believe that either a clear-corneal or pars plana approach can be used, we prefer a scleral-tunnel approach because we feel it is a more secure wound and reduces the chance of postoperative wound leak. This is especially important in children who are more likely to rub or traumatize their eyes postoperatively.

Management of the posterior capsule in pediatric cataract surgery is somewhat controversial in the setting of previous treatment for retinoblastoma. Theoretically, the posterior capsule could act as a barrier to tumor spread if viable tumor cells are present in the eye, and therefore, the posterior capsule should be left intact whenever possible. Nevertheless, it is frequently necessary to perform a primary posterior capsulotomy and anterior vitrectomy, even in the setting of prior treatment for retinoblastoma. Since posterior subcapsular cataract is common after external beam radiotherapy, it is sometimes necessary to remove the posterior capsule in order to clear the visual axis. In our series, four patients underwent a primary posterior capsulotomy and anterior vitrectomy because a dense posterior capsular plaque was noted at the time of surgery. Additionally, we performed primary posterior capsulotomy and anterior vitrectomy in three patients due to the young ages (3.3, 4.3 and 5.4 years) of the children, in whom we anticipated the need for secondary capsulotomy. All five of our patients who did not receive a primary posterior capsulotomy subsequently underwent a Nd:YAG laser capsulotomy. Although some authors advise against primary posterior capsulotomy and anterior vitrectomy in the setting of previously treated retinoblastoma^{13,18}, other studies have shown that a primary posterior capsulotomy and anterior vitrectomy can be performed safely^{9,11}. We believe the risks and benefits of primary posterior capsulotomy and anterior vitrectomy should be considered on a case by case basis, taking into account the location of the cataract, the age of the patient, the availability of the Nd:YAG laser, the length of the quiescent period, and the location and stage of the tumor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1
Pre and postoperative visual acuities as well as length of follow up for the 11 patients who underwent cataract extraction after having had radiation treatment for retinoblastoma

Patient	Preoperative Visual Acuity	Postoperative Visual Acuity	Follow-up (Years)
1 (OD)	Central,Steady,Unmaintained	Counting Fingers at 3 feet	11.3
1 (OS)	20/70	20/50	10.5
2	5/200	20/200	1.15
3	20/80	20/50	1.60
4	20/400	20/40	1.79
5	Central,Steady,Maintained	20/25	12.3
6	20/400	20/200	1.05
7	Light Perception	Hand Motion	6.34
8	Counting Fingers at 6 feet	20/60	4.13
9	Light Perception	Counting Fingers at 2 feet	5.95
10	Light Perception	Hand Motion	6.07
11	20/70	20/60	10.1

OD: Right Eye

OS: Left Eye

Table 2
Literature review of cataract extraction for radiation-induced cataract following retinoblastoma treatment

Author	Year published	Number of Patients (eyes)	Quiescent Interval (range in months)	Procedure (number of eyes)	Length of Follow-up (range in months)	Number of recurrences	Visual Outcomes (number of eyes)
Monge, et al. ¹²	1986	2 (2)	30 months; 72 months	Aspiration; Aspiration + PPV	78 months; 24 months	0	6/18 (2)
Brooks, et al. ¹³	1990	38 (42)	Median = 29 months (17 – 144)	Aspiration; Lensectomy + Ant. Vtx.; pars plicata lensectomy; PPL	Median = 72 months (6 – 178)	3	20/20 – 20/50 (19) 20/80 – CF (12)
Portellos and Buckley ¹¹	1998	8 (11)	Mean = 55 months (16 – 88)	ECCE + capsulotomy + Ant. Vtx. + PCIOL	Mean = 20 months (6 – 39)	0	20/20 – 20/30 (6) 20/50 – 20/250 (5)
Madreperla, et al. ¹⁴	2000	3 (3)	34 months; 9 months; 40 months	Lens aspiration	84 months; 60 months; 189 months	0	20/60 (2) **, HM **
Bhattacharjee, et al. ¹⁵	2003	1 (1)	84 months	ECCE + capsulotomy + PCIOL	144 months	0	20/30
Shanmugam, et al. ¹⁶	2004	(5)	Minimum 24 months	Phaco + capsulotomy + Ant. Vtx. + PCIOL	Not documented	0	> 6/9 (4) at 6 weeks
Sinha, et al. ¹⁷	2004	(9)	Minimum 12 months	Lens aspiration	(24 – 42)	0	No significant improvement noted
Miller, et al. ⁹	2005	12 (16)	Minimum 18 months	ECCE + PPV. + PCIOL	Mean = 66 months (30 – 94)	0	20/20 – 20/40 (11) 20/200 – 20/400 (5)
Honovar, et al. ^{18, £}	2005	34 (34)	Median = 16 months (3 – 54) *	ICCE (1); ECCE (28); PPL (5)	Median = 72 months (12 – 360) *	5	> 20/200 (12)
Moshfeghi, et al. ¹⁹	2005	4 (4)	Mean = 89 months (12 – 172)	Cataract extraction	Mean = 184 months (60 – 339)	1	20/30; CF; HM; Enucleation for recurrence
Payne, et al.	2008	11 (12)	Median = 35 months (17 – 240.0)	ECCE ± capsulotomy ± Ant. Vtx. ± PCIOL	Median = 72 months (13 – 148)	0	VA improved in all eyes with preoperative VA

* Data for all intraocular surgery, including cataract extractions, pars plana vitrectomy and sclera buckling procedures

** Required additional intraocular surgery

£ Data for eleven eyes in this series were also published in the report by Brooks, et al.¹³

Ant. Vtx.- Anterior vitrectomy

ECCE- Extracapsular cataract extraction

ICCE- Intracapsular cataract extraction

PCIOL- Posterior chamber intraocular lens
 Phaco- Phacoemulsification
 PPL- Pars plana lensectomy
 PPV- Pars plana vitrectomy
 VA- Visual acuity