Comment. Yanoff et al\(^4\) and Manschot\(^6\) described the retinoschisis in this disease as occurring in the NFL. Based on histopathologic findings, further postulating that the primary defect might then involve the Muller cells. The OCT findings in our cases suggest that the foveal cystoid separation is not located in the NFL, as described in peripheral retinoschisis,\(^3,6\) but is in the outer plexiform layer. Trese and Foos\(^7\) reported a series of premature infants with infantile cystoid maculopathy resembling X-linked juvenile retinoschisis, in whom gross examination showed cystoid pockets at various retinal layers including deep to the NFL. Azzolini et al\(^8\) reported OCT findings in 3 cases of X-linked juvenile retinoschisis showing a macular cleavage plane in the outer retinal layers as well as in the NFL. Optical coherence tomography provides an in vivo correlation to previous investigations of the histopathologic features of the disease. The OCT findings in this report suggest that the primary abnormality of the fovea in patients with juvenile retinoschisis is actually in the outer retina, specifically in the outer plexiform layer, unlike the peripheral retina, where the schisis is located in the NFL. These findings suggest different developmental mechanisms of retinoschisis in the fovea and peripheral retina. A larger series of OCT imaging in this interesting disease is desirable.

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Financial Disclosure: None.
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Funding/Sponsor: This study was supported by the Research to Prevent Blindness Foundation, New York, NY.


Intraocular Surgery After Treatment of Germline Retinoblastoma

Germline retinoblastoma results from a somatic mutation involving loss or inactivation of the tumor suppressor gene located at 13q14.\(^1\) Absence of gene activity predisposes to retinoblastoma and other tumor development.\(^1,2\) The introduction of chemotherapy protocols with focal consolidation therapy has enhanced our ability to treat germline retinoblastoma while salvaging many eyes that would have been lost previously.\(^3,8\) A secondary benefit has been that we are now preserving eyes with useful vision. However, because of the aggressive, multimodal therapy involved, patients often develop intraocular complications. We evaluated a group of patients who had undergone enucleation for retinoblastoma in one eye with salvage of the other eye and who had maintained tumor quiescence for a period of 12 months or longer in that eye. Our purpose was to determine how these patients fared following intraocular surgery of the salvaged eye.

Patients and Methods. We performed a retrospective review of all germline retinoblastoma cases from January 1, 1985, until December 31, 2000, to identify all patients who had undergone unilateral enucleation with salvage of the other eye. Cases were drawn from the records of the University of Tennessee, Memphis, Department of Ophthalmology, Memphis; the records of the Ophthalmic Oncology Service at St Jude Children’s Research Hospital, Memphis; and the private records of Retina Associates of Florida, Tampa. Cases were enrolled only if the salvaged eye achieved a 12-month period of tumor quiescence and then subsequently underwent intraocular surgery for non–tumor-control reasons. Tumor quiescence was defined as lack of documented tumor growth, lack of vitreous or subretinal seeding, lack of anterior chamber seeding, and lack of metastases. Eligible intraocular surgery included cataract extraction, barrier laser for retinal break, scleral buckle procedure, pars plana vitrectomy, and Nd:YAG laser capsulotomy. Original treatment of the retinoblastoma was recorded, as was the Reese-Ellsworth classification. The 3 primary outcomes were tumor activity, visual acuity, and development of complications. Tumor activity was classified as quiescent, recurrent, and...
extraocular. Tumor recurrence included documented tumor growth or reactivation of the retinoblastoma in the eye (new vitreous seeding, new subretinal seeding, anterior chamber seeding). Extraocular tumor activity included extraocular extension, orbital involvement, and distant metastases. Visual acuity was assessed by Snellen acuity under best-corrected conditions. Nontumor complications were defined as retinal detachment (serous, rhegmatogenous, or tractional), cataract, vitreous hemorrhage, hypotony, elevated intraocular pressure, development of posterior capsular opacification, and epiretinal membrane formation. If the salvaged eye was enucleated, appropriate histopathologic analysis was performed.

**Results.** We identified 110 patients who were treated for retinoblastoma from January 1, 1985, to December 31, 2000. Six cases (5 girls and 1 boy) met the inclusion criteria and form the basis of this report. The average patient age at the time of diagnosis was 9.5 months (median, 8 months; range, 5-21 months). In 3 cases, the left eye was enucleated and in 3 cases, the right eye. The Reese-Ellsworth classification was type V for 3 eyes originally enucleated (Table 1, cases 4-6); for the fellow eyes, the classification was group IIB for 1 and group IVB for 2 (Table 1). The Reese-Ellsworth classification was not known for the patients in cases 1 through 3 because they were treated elsewhere initially. Fellow eye treatment included external beam radiotherapy in all 6 patients (Table 1). In 2 cases the patients underwent simultaneous chemotherapy and in 2 cases plaque brachytherapy labeled with radioactive iodine I 125 was subsequently (Table 1) used.

The average time to first surgery was 85.3 months (median, 85.5 months; range, 12-172 months). The indication for intraocular surgery was cataract in 4 patients and rhegmatogenous retinal detachment in 2 patients. A median of 2.5 additional surgeries (range, 0-5) per eye were needed. The average length of follow-up was 163.7 months (median, 156 months; range, 60-339 months).

Three of the 6 patients demonstrated tumor activity following intraocular surgery (cases 4-6). Two patients (cases 5 and 6) had undergone primary repair of rhegmatogenous retinal detachments while 1 patient (case 4) had undergone cataract surgery (Figure 1 and Figure 2). All 3 cases had pseudohypopyon an average of 13.3 months (median, 10 months; range, 4-26 months) following intraocular surgery. Case 4 underwent enucleation immediately for advanced anterior chamber seed-

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**Table 1. Patient Characteristics Before and After Intraocular Surgery**

<table>
<thead>
<tr>
<th>Patient/Sex/Age at Diagnosis, mo</th>
<th>Reese-Ellsworth</th>
<th>Eye Removed Originally</th>
<th>Fellow Eye Treatment</th>
<th>Quiescence, mo</th>
<th>Surgical Indication</th>
<th>Final Visual Acuity</th>
<th>Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/6</td>
<td>NA</td>
<td>Left</td>
<td>EBRT, chemo</td>
<td>172</td>
<td>Cataract</td>
<td>20/30</td>
<td>339*</td>
</tr>
<tr>
<td>2/M/21</td>
<td>NA</td>
<td>Right</td>
<td>EBRT, chemo (C, D, V), intra-arterial TEM</td>
<td>60</td>
<td>Cataract</td>
<td>CF 4</td>
<td>193*</td>
</tr>
<tr>
<td>3/F/9</td>
<td>NA</td>
<td>Left</td>
<td>EBRT</td>
<td>111</td>
<td>Cataract</td>
<td>HM</td>
<td>142*</td>
</tr>
<tr>
<td>4/F/7</td>
<td>Type V, right eye; type IIVB, left eye</td>
<td>Right</td>
<td>EBRT, I-125</td>
<td>12</td>
<td>Cataract</td>
<td>Enuc</td>
<td>60</td>
</tr>
<tr>
<td>5/F/9</td>
<td>Type IIB, right eye; type V, left eye</td>
<td>Left</td>
<td>EBRT</td>
<td>120</td>
<td>RRD</td>
<td>Enuc</td>
<td>170</td>
</tr>
<tr>
<td>6/F/5</td>
<td>Type V, right eye; type IIVB, left eye</td>
<td>Right</td>
<td>EBRT, I-125</td>
<td>37</td>
<td>RRD</td>
<td>Enuc</td>
<td>78</td>
</tr>
</tbody>
</table>

Abbreviations: C, carboplatin; CF, counting fingers; chemo, chemotherapy; cyclo, cyclophosphamide; D, doxorubicin; EBRT, external beam radiotherapy; Enuc, enucleation; HM, hand motions; I-125, plaque brachytherapy labeled with radioactive iodine I 125; M, methotrexate; NA, not available; RRD, rhegmatogenous retinal detachment; TEM, triethylenemelamine; V, vincristine.

*Treated elsewhere originally. Follow-up represents time from original treatment until last reported examination by one of us.

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**Figure 1.** Active tumor is visible behind the iris in the superonasal quadrant following cataract surgery (case 4).
Three patients had bilateral enucleation and had no vision (Table 1). One patient had a Snellen acuity of 20/30, 1 had counting fingers visual acuity, and 1 had hand motions visual acuity.

Rhegmatogenous retinal detachment was the most frequent nontumor activity complication following intraocular surgery, occurring a total of 4 times in 3 patients without obvious proliferative vitreoretinopathy. Patient 1 developed a rhegmatogenous retinal detachment that was repaired and subsequently re-detached, patient 3 developed a retinal detachment following cataract extraction, and patient 5 developed a sequential retinal detachment following primary repair. One patient developed a tractional retinal detachment following primary repair. One patient developed a tractional retinal detachment (Table 3). Vitreous hemorrhage occurred in 2 cases.

Comment. Current treatment regimens allow for salvage of the contralateral globe and visual function in patients with retinoblastoma. However, as the posttreatment interval increases, we are now being confronted with the long-term complications of these regimens, including late retinal detachment and cataract. The risks and benefits of intraocular surgery to treat these complications have only begun to be defined. In our study, the rate of complications following intraocular surgery was high, with a total of 10 ocular complications and 3 tumor activations in 6 patients. The leading indication for surgery was cataract (n=4) followed by rhegmatogenous retinal detachment (n=2). The leading complication following intraocular surgery was rhegmatogenous retinal detachment (n=4, in 3 patients). In 3 patients, the retinoblastoma reactivated following intraocular surgery after at least 12 months of tumor quiescence. In 2 of these patients, the indication for surgery was rhegmatogenous retinal detachment and in 1 case, cataract removal. All 3 of these patients had anterior chamber pseudohyphopyon, underwent enucleation, and were treated with adjuvant systemic chemotherapy. Despite involvement of an emissary vessel in 1 case and Schlemm canal in 2 cases (1 with the emissary vessel) on histopathologic specimens from the enucleated eyes, there were no cases of macroscopic extraocular extension or metastasis.

The high number of rhegmatogenous retinal detachments is not surprising in that these eyes were subjected to numerous treatments with laser photocoagulation, cryotherapy, and transpupillary thermotherapy. It is likely that the normal vitreoretinal interface was disturbed by both the original treatment and subsequent surgery, resulting in thinning of the retina and atrophic breaks in the retina. While all retinas were eventually reattached, no definite retinal break was identified in any eye with rhegmatogenous retinal detachment.

Other studies have also reported rhegmatogenous retinal detachment following retinoblastoma treatment; although the retina was successfully reattached in many patients in these studies, other attempts at reattachment were unsuccessful and were followed by adverse sequelae in some cases. Madreperla and colleagues identified retinal breaks in 2 of 4 cases of late rhegmatogenous retinal detachment after successful treatment of retinoblastoma. Using vitreoretinal surgical techniques, they achieved successful reattachment in 3 cases without tumor re-
Not all studies reported negative sequelae from intraocular surgery following treatment of retinoblastoma. A study by Portellos and Buckley\textsuperscript{12} reported on 11 eyes in 8 patients who successfully underwent cataract extraction and intracocular lens implantation following treatment of retinoblastoma. The study included 4 patients with bilateral disease and 4 patients with unilateral disease. Nine eyes underwent primary and 2 underwent secondary intracocular lens implantation. The mean time from conclusion of external beam radiotherapy to cataract extraction was approximately 55 months (4.6 years). No eye developed tumor recurrence, extraocular spread, retinal detachment, or radiation retinopathy in this cohort. This study represents the second longest quiescent interval between tumor treatment and intracocular surgery, and it seems to indicate that cataract surgery is relatively safe.

In our study, cataract was the indication for surgery in 4 patients, with 1 patient developing tumor reactivation and undergoing enucleation. Two of 2 eyes undergoing primary intervention for rhematogenous retinal detachment with vitrectomy reactivated and underwent enucleation. Interestingly, the 2 eyes that developed rhematogenous retinal detachment following cataract surgery and underwent repair with vitrectomy did not have tumor reactivation.

In reviewing the data from our study and the previous reports,\textsuperscript{9,11} we are left to conclude that development of rhematogenous retinal detachment is an ominous sign for both visual acuity and eye salvage. It is possible that development of rhematogenous retinal detachment may herald occult reactivation of the retinoblastoma. In this instance, tumor reactivation could place mechanical stress upon the retina, resulting in stretching of an already damaged tissue and allowing microscopic breaks to form and sub-sensory fluid to accumulate. Likewise, it is possible that surgical repair of retinal detachment reactivates dormant or incompletely eradicated tumor cells with an infusion of nutrients into the vitreous cavity.

In this case series of aggressive germline retinoblastoma where one eye was originally enucleated and the second eye noted to have no tumor activity for a median of 85.5 months, tumor reactivation occurred in 3 of 6 cases following primary repair of rhematogenous retinal detachment with vitrectomy. Our experience is similar to that of earlier studies with less aggressive tumors and shorter tumor-quiescence intervals. Additionally, cataract surgery resulted in tumor reactivation in 1 of 4 cases. The rate of postsurgical complications was high, particularly the development of rhematogenous retinal detachment. No case of extraocular tumor spread or metastasis was noted. We recommend that surgical intervention in patients with these types of germline retinoblastoma be undertaken with due consideration for the risk of tumor reactivation and enucleation, even after lengthy tumor-quiescence intervals.

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Idiopathic CD4+ Lymphocytopenia and Sjogren Syndrome

Idiopathic CD4+ lymphocytopenia (ICL) is a rare syndrome that is marked by a CD4+ count that is less than 300 cells/mm³ without human immunodeficiency virus infection.1 Its course differs from that of AIDS in that although patients with this disorder may develop opportunistic infections, the majority of them remain stable. No transmissible agent has been implicated in the pathogenesis of ICL. The ocular manifestations of ICL have only rarely been described,2 and there are no reports of ICL in ophthalmology literature. We report the case of a patient with ICL and Sjogren syndrome.

Report of a Case. A 52-year-old woman was referred to the ophthalmology department because of a several-year history of burning and stinging in both eyes. Her medical history was significant for ICL, with 5 CD4+ counts during 6 years ranging from 93 to 253, despite 3 negative human immunodeficiency virus test results. Additionally, assays for Epstein-Barr virus, cytomegalovirus, and human herpesviruses 6 and 8 were all negative. At the time, her visual acuity was 20/20 OD and 20/25 OS. The patient had marked superficial punctate keratitis and abundant mucus production in both eyes, and as a result, she began a course of applying artificial tears to both eyes every 2 hours with only minimal relief.

During the ensuing months, a bandage contact lens was placed over the patient's left eye, but it failed to relieve her symptoms. Schirmer testing with topical anesthesia showed 6 mm of tearing in the right eye and 5.5 mm in the left. Subsequent bilateral inferior punctal plug placement provided some relief, but her symptoms and superficial punctate keratitis persisted. In addition to the aggressive use of artificial tears, other modalities (corticosteroid eye drops and systemic doxycycline administration) were employed, but the patient's condition did not improve.

A diagnosis of Sjogren syndrome was confirmed after testing showed a Sjogren syndrome antigen antibody level of 13.1 (range, 0-4.9 U/mL). The patient then began a course of cevimeline hydrochloride (30 mg by mouth 3 times a day), and her symptoms improved considerably. Furthermore, her superficial punctate keratitis diminished appreciably. She remains stable and comfortable on this regimen with the use of artificial tears 4 times per day.

Comment. Idiopathic CD4+ lymphocytopenia is a rare disorder of CD4+ lymphocytopenia without human immunodeficiency virus infection. The ophthalmic sequelae of this syndrome have not yet been elucidated. In this report, we describe the characteristics and clinical courses of a patient with ICL and Sjogren syndrome.

The underlying pathophysiology of ICL results from apoptosis of CD4+ cells,3 with subsequent limitations on the repertoire of the T-cell population.4 Autoimmune processes such as Sjogren syndrome may result from restriction of T-cell diversity, which may lead to a subsequent decrease in immune surveillance. This scenario would allow autoantibodies that may otherwise be cleared from systemic circulation to flourish. Kirtava et al2 found an increased prevalence of ICL among patients with Sjogren syndrome.

In summary, both ophthalmologists and internists should be aware of the connection between Sjogren syndrome and patients with ICL. Further evaluation is necessary to determine other ocular manifestations of ICL.

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Advanced Keratomalacia With Descemetocoele in an Infant With Cystic Fibrosis

Xerophthalmia refers to the spectrum of ocular manifestations of vitamin A deficiency. It represents the leading cause of childhood blindness worldwide but is uncommon in industrialized countries, where xerophthalmia is more often the result of malabsorption than malnutrition due to poverty. Cystic fibrosis (CF) is an autosomal recessive disease with hyperviscosity of mucus secretions causing chronic pulmonary changes and pancreatic insufficiency. Anderson2 was the first to note the association between xerophthalmia and CF, now thought to be due to fat malabsorption resulting in fat-soluble vitamin deficiency. Advanced xerophthalmia has been reported as an initial sign of CF.3,4 A recent review article3 summarized the ocular findings of CF to include xerophthalmia, tear film abnormalities, papilledema, and nystagmus. To our knowledge, this is the first clinicopathologic report of keratomalacia with a descemetocoele requiring keratoplasty as the initial manifestation of CF.

Report of a Case. A 5-month-old girl from Juarez, Mexico, was admitted to a hospital in Las Cruces, NM, with...