Visual Outcome after Intravenous Chemotherapy for Retinoblastoma

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Retinoblastoma is recognized by the presence of unifocal or multifocal yellow-white retinal tumors in young children, often associated with subretinal fluid and vitreous and subretinal tumor seeds. Occasionally, subretinal and vitreous hemorrhage are noted.[1,2] These features not only endanger the child's life, but also threaten the globe, leading to a concern for enucleation or poor visual acuity.[2,4]

In the past, treatment strategies for retinoblastoma relied heavily on external beam radiotherapy (EBRT) and enucleation. Today, these methods are reserved for only the most advanced cases in which standard treatment fails. Standard treatment includes one or more of the following chemotherapy strategies: intravenous chemoreduction, intraarterial chemotherapy, sub-Tenon chemotherapy, and, rarely, intravitreal chemotherapy.[2] Following chemotherapy, regressed retinoblastoma is consolidated at each visit with transpupillary thermotherapy if the tumor is postequatorial, cryotherapy if the tumor is anterior to the equator, and plaque radiotherapy if substantial tumor recurrence is detected.[1-3] Despite these efforts to save the eye, there have been only a few reports on visual outcomes. Herein, we describe a case of retinoblastoma treated with intravenous chemoreduction and focal methods and discuss visual outcomes.

CASE

A 13-month-old white female was noted by parents to have heterochromia and leukocoria in the right eye (OD). Examination revealed visual acuity of no fix and follow in the OD and fix and follow in the left eye (OS). Intraocular pressure was 11 mm Hg OD and 16 mm Hg OS. Diffuse iris neovascularization OD was detected.

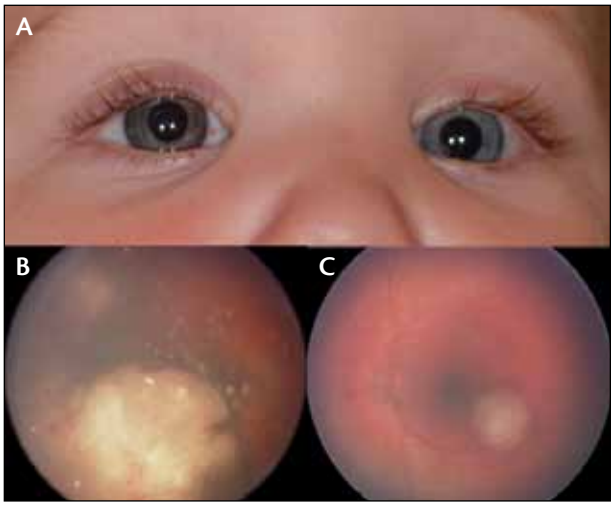

Figure 1. Findings in both eyes before treatment. Heterochromia from diffuse iris neovascularization OD (A). The right eye showed extensive retinoblastoma with 4 large tumors, shallow retinal detachment, and extensive vitreous and subretinal seeds (B). The left eye showed ICRB group B retinoblastoma with 1 macular and 1 extramacular exophytic lesion (C).

Funduscopically, there were 4 retinoblastomas OD with shallow retinal detachment and extensive vitreous and subretinal seeding (Figure 1). The left eye revealed 2 retinoblastomas, each with basal diameter approximately 3 mm. These findings were consistent with bilateral retinoblastoma, labeled as group E OD and Group B OS according to the International Classification of Retinoblastoma (ICRB).

Due to the risk for invasive retinoblastoma, high risk for recurrence, and poor visual prognosis, enucleation

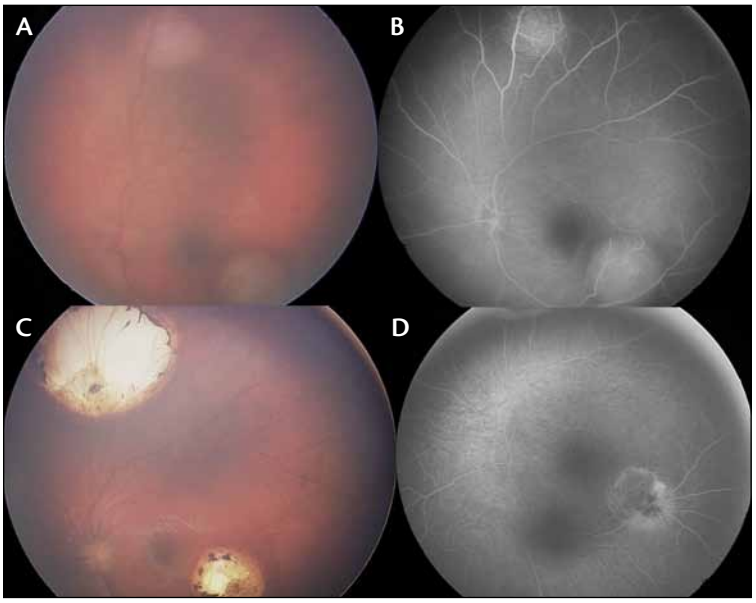

Figure 2. Left eye before and after chemoreduction. Before chemoreduction (A). The left eye showed 2 small retinoblastomas with one at the equator and 1 in the macular region, both showing hyperfluorescence on angiography (B). After chemoreduction (C). Following chemoreduction and cryotherapy to the equatorial tumor and thermotherapy to the macular tumor, the eye shows flat regressed hypofluorescent scars (D). Final visual acuity was 20/25 OS.

was performed OD. The left eye was treated with 6 cycles of intravenous chemoreduction using vincristine and carboplatin. Etoposide was not employed. Tumor scar consolidation with repetitive transpupillary thermotherapy and/or triple freeze-thaw cryotherapy was applied. Transient serous retinal detachment following thermotherapy was noted 2 mm from the foveola. The treated tumors achieved Type IV regression. On 6-year follow-up, tumor scars remained stable and uncorrected visual acuity was 20/25 OS (Figure 2).

DISCUSSION

Intravenous chemoreduction is remarkably effective in controlling retinoblastoma, particularly in eyes with moderate or less advanced disease. In an analysis of 249 eyes with retinoblastoma, Shields et al[5] found a six-cycle regimen of vincristine, etoposide, and carboplatin plus focal tumor consolidation successful in controlling 100% of ICRB group A eyes, 93% of group B, 90% of group C, and 47% of group D eyes. Chemoreduction has replaced EBRT in the management of retinoblastoma.

TABLE 1. VISUAL OUTCOME IN EYES WITH RETINOBLASTOMA TREATED WITH CHEMOREDUCTION. A COMPARISON OF MACULAR VERSUS EXTRAMACULAR TUMORS.

	Narang et al[8]		Demirci et al[7]	
	n = 140 eyes		n= 54 eyes	
	Macular tumor	Extramacular tumor	Macular tumor	Extramacular tumor
	n = 105	n = 35	n = 33	n = 21
VA ≥ 20/40 n (%)	23 (22%)	32 (91%)	8 (24%)	19 (90%)
VA ≥ 20/200 n (%)	na	na	15 (45%)	21 (100%)
VA=visual acuity, n=number, na=not applicable, as this paper did not distinguish beyond VA ≥ 20/40.				

TABLE 2. VISUAL OUTCOME IN EYES WITH RETINOBLASTOMA TREATED WITH CHEMOREDUCTION. FACTORS PREDICTIVE OF VISUAL ACUITY OF 20/40 OR BETTER.

Factors	P Value	Relative Risk	Odds Ratio
Demirci et al[7]			
Tumor margin from foveola, ≥3 mm vs <3mm	0.009	14.5	na
Subretinal fluid at initial examination, absent vs present	0.009	14.5	na
Narang et al[8]			
Subfoveolar tumor	0.049	na	5.334
Number of tumors	0.027	na	0.188
na=not applicable, as this statistical analysis was not performed in the original study.			

Often, multiple tumors are noted in patients with familial retinoblastoma who are screened for the disease at birth. This allows early detection and resultant good visual acuity.

Side effects of radiation-related cataract, retinopathy, dry eye, and facial hypoplasia are avoided with chemoreduction.[5] Turaka et al[6] recently reported on long-term follow-up of children with germline mutation retinoblastoma treated with chemoreduction and found that the risk for second cancers was notably low in this group at only 4%, compared with far greater historical risk for those treated with EBRT. In fact, the cumulative incidence of second cancers in 45 germline mutation patients treated with chemoreduction and EBRT was 21% vs only 4% in the 142 patients treated with chemoreduction alone.[6] The impact of EBRT on the development of second cancers is unquestionable.

Demirci et al[7] studied visual results following chemoreduction for retinoblastoma. In that study of 54 eyes, 5-year follow-up showed visual outcome of 6/12 or better in 50% of eyes and 6/60 or better in 67% (Tables 1 and 2). Of those patients with bilateral retinoblastoma, 74% manifested final visual acuity of 6/12 or better in at least 1 eye, and 87% measured 6/60 or better in at least 1 eye. There were 2 factors predictive of good visual outcome: extramacular tumor location (greater than 3 mm from the foveola) and absence of subretinal fluid.[7] Eyes with tumors within the macular region achieved visual acuity of 6/12 or better in 24% and 6/60 or better in 46% of cases. In contrast, eyes with extramacular retinoblastoma showed visual acuity of 6/12 or better in 90% and 6/60 or better in 100% of cases.

Narang et al[8] examined 140 eyes following chemoreduction for retinoblastoma and found that 71% achieved a visual acuity of 6/60 or better and 37% reached 6/12 or better. The authors noted a mean 57% decrease in tumor basal diameter and 42% decrease in thickness after chemoreduction, and they commented that this reduction was important in clearing retinoblastoma in the macular region and allowing return of visual acuity. By multivariate analysis, the 2 factors predictive of good visual acuity (6/12 or better) were absence of subfoveolar tumor and greater number of tumors (Tables 1 and 2). Eyes with subfoveolar tumors resulted in visual acuity of 6/12 or better in only 6% of cases, compared with those without subfoveolar tumors that achieved 6/12 or better in 67% of cases. Interestingly, the presence of multiple tumors was predictive of better visual outcome. Eyes with multiple tumors generally had smaller tumors with mean diameter of 9.8 mm, compared with 12.2 mm in those with a single tumor. Often, multiple tumors are noted in patients with familial retinoblastoma who are screened for the disease at birth. This allows early detection and resultant good visual acuity.

In our patient, there was macular involvement with retinoblastoma 2 mm from the foveola. Following chemoreduction and cautious, fovea-sparing thermotherapy, the scar remained 2 mm from the foveola and the visual acuity was 20/25. We anticipate that this child will have a paracentral scotoma.

In summary, this case illustrates some important facts about chemoreduction including the high rate of tumor control and the lack of ocular complications with resultant excellent visual acuity. Chemoreduction continues to play an important role in the management of bilateral retinoblastoma. ■

Support provided in part by the Carlos G. Bianciotto Fund for Eye Cancer Research, Philadelphia, PA (CLS), the Lucille Wiedman Fund for Pediatric Eye Cancer, Philadelphia, PA (CLS), Lift for a Cure, Morrisdale, PA (CLS), and the Eye Tumor Research Foundation, Philadelphia, PA (CLS).

The authors have no financial interest in the devices or medications in this document.

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