



## Cyst-like recurrence of retinoblastoma diagnosed by multimodal imaging

Noy Ashkenazy<sup>a</sup>, J. Daniel Diaz<sup>a</sup>, Eric D. Hansen<sup>a,b</sup>, J. William Harbou<sup>a,c,d</sup>, Zelia M. Correa<sup>a,c,\*</sup>

<sup>a</sup> Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, FL, USA

<sup>b</sup> John A. Moran Eye Institute, University of Utah, Salt Lake City, UT, USA

<sup>c</sup> Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, USA

<sup>d</sup> University of Texas Southwestern Medical Center, Dallas, TX, USA

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### ABSTRACT

**Purpose:** To illustrate the diagnosis and management of an atypical, cyst-like recurrence of retinoblastoma.

**Observations:** A 4-month-old boy was diagnosed with Group B retinoblastoma in the right eye, consisting of a 10 × 9 × 3.6 mm retinal tumor temporal to the macula. He was treated with one session of intra-arterial ophthalmic artery chemotherapy using melphalan, followed by three sessions of diode laser transpupillary thermotherapy (TTT), after which complete tumor regression was achieved. 45 weeks after initial treatment, a cystic lesion was detected adjacent to superior margin of the regressed tumor scar. The differential diagnosis included pigment epithelial detachment, retinal gliosis, secondary retinoschisis, and local tumor recurrence. Multimodal imaging including OCT angiography confirmed the diagnosis of local recurrence manifesting as a vascularized cyst-like lesion. Two additional sessions of TTT achieved sustained tumor regression through 16 months of additional follow-up.

**Conclusions and Importance:** Recurrence of retinoblastoma following chemotherapy typically manifests as enlargement of a previously regressed tumor, or seeding into the vitreous or subretinal space. An unusual cyst-like recurrence of retinoblastoma at the margin of a previously regressed tumor was diagnosed by multimodal imaging. Focal diode laser transpupillary thermotherapy was curative.

### 1. Introduction

Retinoblastoma is the most common pediatric eye cancer and can occur via hereditary transmission of a germline *RB1* mutation in ~40% of cases.<sup>1</sup> Treatment options include laser photocoagulation, cryotherapy, brachytherapy, enucleation, and intravenous, intra-arterial, and intravitreal chemotherapy (IAC). IAC involves selective catheterization of the ophthalmic artery to infuse chemotherapeutic agents, most commonly melphalan, carboplatin, and topotecan.<sup>2</sup>

Prompt identification of tumor recurrence is important to assure local control and prevent disease progression. Here, we present a rare case of cyst-like marginal recurrence of retinoblastoma that was diagnosed with multi-modal imaging and successfully treated with transpupillary thermotherapy (TTT).

### 2. Methods

A retrospective review of a single clinical case was performed, in compliance with the tenants of the Declaration of Helsinki.

### 3. Findings

#### 3.1. Case report

A four-month-old boy was referred for right leukocoria noted by the child's parents for one week. Examination under anesthesia (EUA) revealed intraocular pressures of 13 mmHg and 16 mm Hg in the right and left eye, respectively. Anterior segment examination was normal bilaterally. The patient was diagnosed with unilateral Group B retinoblastoma in the right eye. The tumor measured 10 × 9 × 3.6 mm and was located in the temporal macula (Fig. 1). Germline testing for *RB1* was negative. Baseline MRI brain and orbits was normal. The patient was treated with one session of IAC using melphalan (4.8 mg), which resulted in marked tumor regression. He was then treated with three sessions of consolidative diode laser TTT using an 810 nm diode laser (IRIDEX, Mountain View, CA) at four to six-week intervals, after which complete clinical tumor regression was achieved (Fig. 1).

At 45 weeks after initial treatment, however, a new cyst-like lesion was identified at the superior margin of the regressed tumor scar, which

\* Corresponding author. Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, 900 N.W. 17th Street, Miami, FL, 33136, USA.

E-mail address: [zcorrea@med.miami.edu](mailto:zcorrea@med.miami.edu) (Z.M. Correa).

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was evaluated with RetCam fundus photography and fluorescein angiography (RetCam, Clarity Medical Systems), posterior B-scan ultrasonography (Aviso, Quantel Medical by Lumibird, Poland), and optical coherence tomography (OCT) and angiography (OCTA) (Spectralis, Heidelberg Engineering, Germany) (Fig. 2). Multimodal imaging was consistent with cyst-like vascularized retinal tumor. After two additional sessions of TTT (500–1000 mW, continuous application) to the base and borders of the recurrent lesion, the cyst collapsed and complete tumor regression was achieved. There has been no subsequent recurrence through 16 months of follow up.

#### 4. Discussion

Understanding how to best achieve successful tumor regression and avoid of tumor recurrence is a major concern when treating retinoblastoma.<sup>3</sup> In 2019, Berry et al. classified retinoblastoma recurrence patterns into retinal, vitreous seeds, subretinal seeds, anterior segment, and extraocular (iatrogenic).<sup>4</sup> Retinal recurrence of retinoblastoma has been described in up to 23% of cases treated with IAC. As in our case, the majority of recurrences present within three years of diagnosis.<sup>4,5</sup> Risk factors for recurrence include the presence of subretinal seeds, germline *RB1* mutation, macular or inferior tumor location, male gender, and tumor thickness over 3 mm.<sup>4,6,7</sup> The patient in this report possessed the latter three risk factors.

Most local recurrences adjacent to a previously treated tumor present as one or more solid nodular lesions. In our case the recurrence was characterized by a cyst-like structure, with a differential diagnosis of secondary retinoschisis and pigment epithelial detachment. Multimodal imaging allowed the correct diagnosis to be made at first detection without the need for an observation period, thereby allowing prompt and effective treatment. The use of fluorescein angiography and OCT angiography confirmed that the lesion was arising from the retina and revealed abnormal intralesional blood vessels consistent with neoplastic tissue (Fig. 2). To our knowledge, a cyst-like recurrence of retinoblastoma has not been previously described in the literature.

Treatment options for local retinoblastoma recurrence following IAC include TTT, cryotherapy, intravitreal chemotherapy, additional IAC,

plaque radiotherapy, external beam radiotherapy, and enucleation.<sup>8</sup> In a series of 22 eyes, Abramson and Scheffler concluded that retinoblastoma tumors smaller than 1.5 disc diameters in size were successfully treated with TTT alone, with globe preservation occurring in 92% of cases.<sup>9</sup> Consistent with these findings, the small cyst-like marginal recurrence and the two satellite lesions in our clinical case were converted to tumor scars following TTT covering 100% of the tumor foci. We prefer treating with TTT when feasible, as it is associated with a lower risk of complications than other options.

#### 5. Conclusion

We illustrate a distinctive case of retinoblastoma with unusual post-IAC local recurrence, characterized by a cyst-like structure comprising atypical vascularized retinal tissue. Multimodal imaging distinguished this diagnosis from other simulating lesions, leading to prompt and effective treatment with TTT.

#### Funding

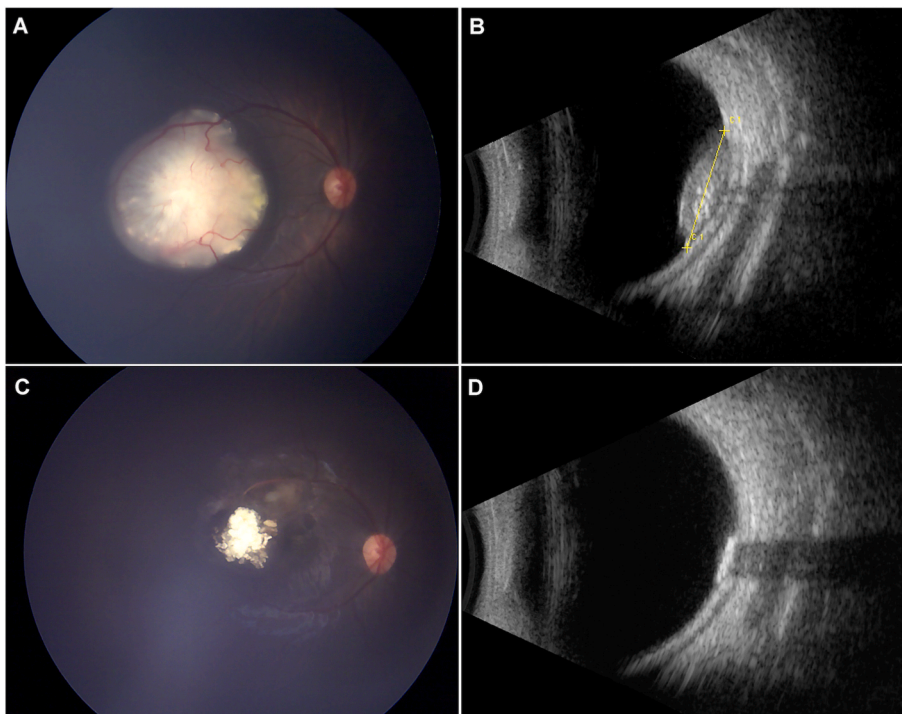
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#### Authorship

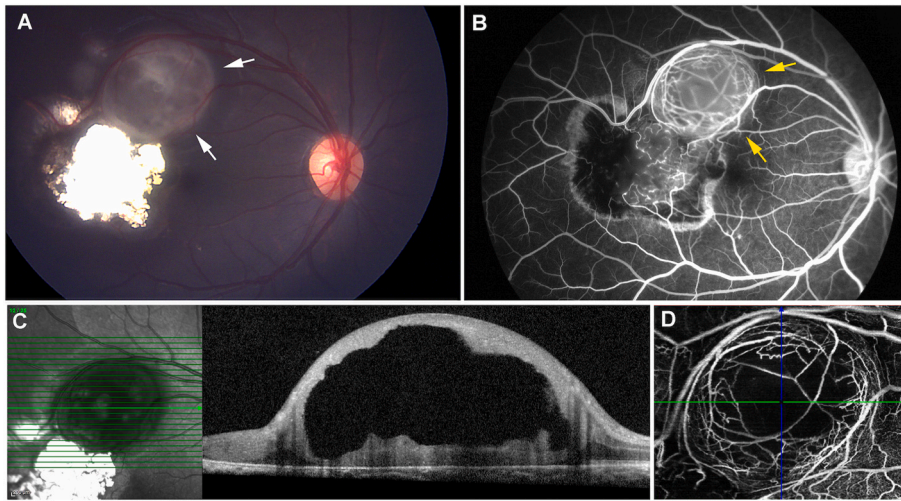
All authors attest that they meet the current ICMJE criteria for Authorship.

#### Patient consent

This case report does not contain any personal information that could lead to the identification of the patient.



**Fig. 1.** Initial presentation of unilateral retinoblastoma. A. At presentation, fundus photography (RetCam, Clarity Medical Systems) showed a white vascularized retinal tumor in the temporal macula. B. At presentation, B-scan ultrasonography (Aviso, Quantel Medical) revealed an elevated retinal tumor measuring 10 × 9 × 3.6 mm with intralesional calcifications and intrinsic vascularity. C. At 21 weeks after one session of intra-arterial chemotherapy with melphalan, followed by three sessions of diode laser transpupillary thermotherapy, the tumor was markedly regressed. D. Ultrasonography at that time demonstrated a plaque-like calcified tumor remnant with no evidence of residual viable tumor.



**Fig. 2.** Multimodal imaging of cyst-like tumor recurrence. A. At 45 weeks after initial treatment, a cyst-like retinal lesion (arrows) was identified at the superior edge of the regressed primary tumor. B. Fluorescein angiography demonstrated abnormal vascularity and leakage within the cystic lesion, which appeared arise from a vascularized remnant at the nasal edge of the original tumor. C. Optical coherence tomography (OCT) (Spectralis, Heidelberg Engineering, Germany) showed that the cyst-like lesion consisted of an irregularly thickened floor and dome-shaped roof, with effacement of the normal retinal layers. D. OCT angiography (OCTA) demonstrated that the abnormal blood vessels were located mostly within the roof of the lesion within the superficial vascular complex.

### Declaration of competing interest

None of the authors have any financial disclosures relating to the content of this article.

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