Indications for treatment include decreased vision, ocular discomfort, inadequate view of the posterior segment, or unsatisfactory appearance.[3]

BK after ROP treatment was first described by Hittner and colleagues[4] in 1979. Here we present the largest known case series of BK after diode treatment of ROP, with 10 affected patients, or 2.94% of all patients lasered during the same time period. Other published case series cite an incidence of 1.09% (2/184)[5] to 6.45% (2/31).[6]

The etiology of BK after ROP laser treatment is unclear. Salgado and colleagues[5] hypothesized the presence of anterior segment ischemia and inflammation after laser treatment as a predisposing factor. Multiple other studies have suggested the presence of anterior segment ischemia based on the presence of cataracts, iris synechiae, corneal opacification, iris atrophy, and shallow anterior chambers.[7-10] Kaiser and Trese[10] proposed that the mechanism for anterior segment ischemia after retinal laser may be a combination of impairment of blood flow in the long posterior ciliary arteries from scleral depression and confluent tissue ablation.

Salgado and colleagues[5] also noted that prethreshold versus threshold ROP had a higher rate of anterior segment complications and lower mean postmenstrual age of treatment (36.6 weeks for prethreshold vs 37.9 weeks for threshold). Our cohort had an average postmenstrual age of 36.78 $\pm$ 1.15 weeks at treatment, which may be associated with a higher rate of anterior segment complications.

In our series, only 1 patient had low-grade anterior chamber inflammation, noted 10 years after ROP laser; another patient exhibited posterior synechiae and flare without inflammation. Although it is difficult to determine the precise etiology of BK, we hypothesize that diode laser treatment could predispose these eyes to BK by laser-induced anterior segment ischemia or from subclinical post-laser inflammation. Anterior segment ischemia may be more common with a confluent pattern of laser therapy often seen with ROP diode laser treatments.[3-7] Furthermore, many patients with prematurity may display a narrow anterior chamber angle because of arrested development of the anterior segment, as hypothesized by Fledelius and colleagues.[9] The narrowing of the anterior chamber could be associated with intermittent angle closure, elevated intraocular pressure, and secondary anterior chamber inflammation. This narrowing of the angle was seen in 4 of our patients (6 eyes), and 1 of our patients was ultimately diagnosed with narrow angle glaucoma.

BK may be an underreported complication of ROP laser treatment that can be associated with younger postmenstrual age at treatment, anterior segment ischemia, post-laser inflammation, or long-term intermittent angle closure. Continued monitoring of patients with BK is necessary; half our patients required treatment. Although this case series is limited by its retrospective nature, it emphasizes the importance of long-term follow-up of post laser ROP patients for late-onset BK and possible risk of narrow-angle glaucoma.

### Literature Search

PubMed search was last performed in April 2019 using search terms *band keratopathy* and *retinopathy of prematurity*, without language or date restrictions.

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# Personalized pediatric ophthalmology: a case report


**Lillian K. To, MD, MS,[a] Parth R. Shah, MBBS, FRANZCO,[a] Hannah L. Scanga, MS, LCGC,[a] Alexis L. Franks, MD,[b] Franklyn P. Cladis, MD,[c] and Ken K. Nischal, MD, FRCOphth[a]**

*Author affiliations: [a]UPMC Eye Center, [b]Department of Pediatrics, Division of Child Neurology, and [c]Department of Anesthesiology, UPMC Children's Hospital of Pittsburgh, and University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania*



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*Correspondence: Ken K. Nischal, MD, FRCOphth, Children's Hospital Way, 4401 Penn Ave., Floor 3, Penguin Pod, Pittsburgh, PA 15224 (email: nischalkk@upmc.edu).*



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**The availability of genetic sequencing has given physicians a new tool for diagnosis and treatment of disease, and "personalized medicine" has become an increasingly common term in general but not in pediatric ophthalmology. We present a case of a toddler who developed ataxia, opsoclonus, myoclonus, and developmental regression following anesthesia for a common otolaryngology procedure. The child was found to have a variant in the *MT-ND6* gene (m.14484T>C), most commonly associated with Leber hereditary optic neuropathy, despite a phenotype more closely resembling Leigh syndrome. The incongruence of phenotype and genotype prompted whole exome sequencing, which identified an unexpected intronic missense mutation in *RB1* (1960+5G>A), with a 90% penetrance for retinoblastoma. Limited evaluation of the posterior pole in clinic did not identify any lesions, and the risks and benefits of examination under anesthesia were discussed among neurology, ophthalmology, and anesthesiology. We report the outcome of these discussions. The value and risks of personalized medicine are discussed.**

## Case Report

An 18-month-old boy was seen at the Ophthalmology Department of UPMC Children's Hospital, Pittsburgh, Pennsylvania, and had a normal examination. His past medical history revealed normal developmental milestones until the age of 12 months, when he developed transient abnormal rapid multidirectional eye movements after undergoing general anesthesia for bilateral tympanostomy tube placement for recurrent ear infections. He subsequently experienced substantial clinical deterioration and developed ataxia, opsoclonus, and myoclonus along with language and motor regression. Brain magnetic resonance imaging (MRI) was interpreted as normal, and based on clinical signs an initial diagnosis of opsoclonus-myoclonus-ataxia syndrome (OMA) was made. Treatment with pulse-dose dexamethasone and intravenous immunoglobulin led to some initial improvement, but further neurologic and developmental regression occurred during episodes of viral illness and after anesthesia exposure for follow-up imaging. Given the atypical clinical course for OMA, an ataxia gene panel (NGS324.9 Ataxia/Episodic Ataxia Disorders, 117 genes [MNG Laboratories, Atlanta, GA]) revealed a homoplasmic pathogenic variant in the *MT-ND6* gene (m.14484T>C), a primary mutation for Leber hereditary optic neuropathy (LHON). As a male, this carries a penetrance of 40%-50% variable by age.[1] Relatives were not tested based on family preference.

The patient's signs were uncharacteristic for LHON. Additionally, his multiple regressive episodes and finding of mild posterior white matter hyperintensity on a follow-up brain MRI prompted concern for possible Leigh syndrome. Trio exome sequencing (GeneDX, Gaithersburg, MD) was performed to evaluate other nuclear genes for variants. This test failed to reveal a cause of the patient's clinical presentation but incidentally uncovered a heterozygous known pathogenic intronic variant in *RB1* (1960+5G>A),[2,3] which has a >90% lifetime risk for retinoblastoma.[4,5] The father was found to have mosaicism for the same variant, and the patient's only younger sibling underwent targeted variant analysis for *RB1* and was negative.

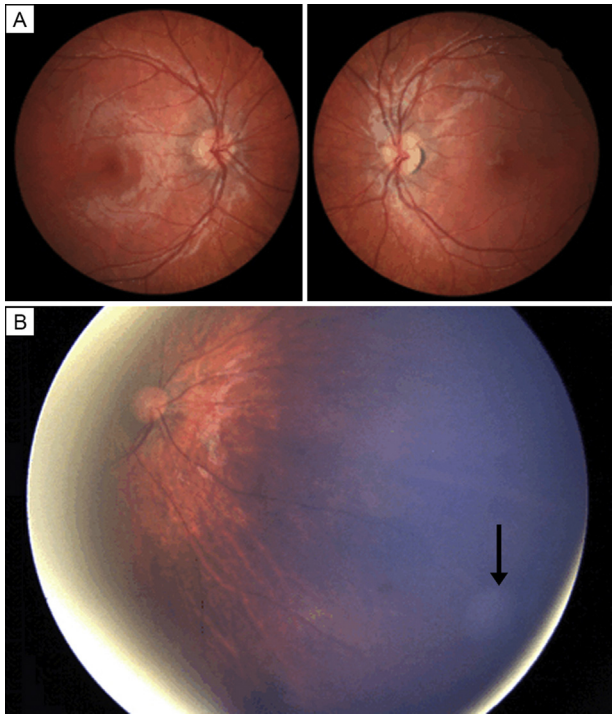


**FIG 1.** A, Bilateral fundus photographs showing healthy posterior pole. B, Small solitary retinoblastoma seen in the right nasal periphery at examination under anesthesia (black arrow).

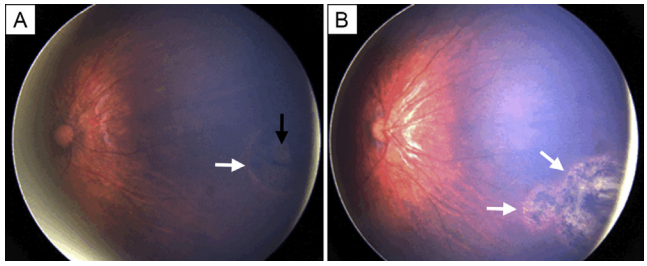


**FIG 2.** A, Residual retinoblastoma (black arrow) within area of cryotherapy scar (white arrow). B, Eight months after initial treatment, the cryotherapy scar is seen (white arrows), with no recurrence of tumor. Note retinal elevation seen inferior to the scar is from scleral indentation.

Repeat ophthalmic examination at 36 months of age yielded a normal view of the bilateral posterior poles (Figure 1A) and normal B-scan ultrasonography. After much deliberation between neurology, ophthalmology, and anesthesiology to weigh risks of examination under anesthesia versus risk of undiagnosed retinoblastoma, the child underwent examination under anesthesia at 37 months. A personalized anesthetic regime was formulated using sevoflurane and nitrous oxide, with careful avoidance of hypoglycemia.

A small retinoblastoma (<1 disk diameter) was found at 4 o'clock in the right peripheral retina, close to the ora serrata (Figure 1B). Triple freeze-thaw cryotherapy was applied due to the anterior location, and the child was re-examined under anesthesia 6 weeks later. Within the cryotherapy scar, residual tumor was seen and was treated with repeat cryotherapy (Figure 2A). Two further examinations under anesthesia revealed no recurrence or new tumors, with last follow-up 8 months after the first treatment (Figure 2B). The patient tolerated the procedures well, with no regression after anesthesia.

## Discussion

It is likely that, had this child's tumor not been found through information at hand, he would have presented later in a more serious and less manageable condition.[2] Screening for high-risk tumors includes examination under anesthesia beginning at 8 weeks of age, with monthly examinations until age 1 year and subsequently every 2 months from 1 to 2 years, every 3 months from 2 to 3 years, every 4 months from 3 to 4 years, and every 6 months from 4 to 5 years.[6] Examinations can be performed without anesthesia in cooperative older children. The location of retinoblastoma tumors is correlated with the maturation process of the retina, with tumors becoming increasingly peripheral with age.[7] After 2 years of age, 50% of detected tumors are found in the far periphery; this trend led us to pursue a definitive diagnostic procedure.

In patients with known mitochondrial disorders, anesthesia principles include reducing mitochondrial stress through avoidance of metabolic acidosis, hypothermia, hypoglycemia, catabolism, and hypovolemia as well as minimizing pain, anxiety, nausea, and vomiting.[8] In our center, propofol is generally avoided, because prolonged use can result in metabolic acidosis, even in patients without baseline mitochondrial disorders.[9] During the patient's prior procedures, propofol was used for induction and maintenance. Of the volatile agents, sevoflurane in children with mitochondrial disorders undergoing muscle biopsy, with a mean anesthetic duration of 36 minutes, shows a good safety profile.[10]

The ambiguity of the actual mitochondrial disorder (LHON versus Leigh syndrome)[11] led to WES, which illustrates the expanding role of genetic testing in diagnosis and treatment of disease. Utilization of this technology requires the physician to play a crucial role in helping patients and families to understand and comprehend the advantages and liabilities of the complex information. Considerations include, but are not limited to, identification of variants of unknown significance, unmasking adult-onset disease in a pediatric population, discovery of disease with high familial penetrance, and identification of nonpaternity or consanguinity.

The study of genetics is increasingly incorporated in everyday medicine. With appropriate interdisciplinary discussion, outcomes can improve drastically in cases where genetic diagnoses inform ophthalmological examination and treatment. Pediatric ophthalmologists must continue to adapt to the unique challenges of these new directions.

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# Successful treatment of an exudative choroidal hemangioma with oral propranolol in a 10-year-old boy


**Bliss E. O'Bryhim, MD, PhD,[a] Albert S. Li, MD,[a] Susan J. Bayliss, MD,[b] Lawrence Tychsen, MD,[a,c]**

*Author affiliations: [a]Department of Ophthalmology and Visual Sciences, Washington University in St. Louis, St. Louis, Missouri; [b]Department of Dermatology, St. Louis Children's Hospital, St. Louis, Missouri; [c]Department of Pediatrics, St. Louis Children's Hospital, St. Louis, Missouri*



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*Correspondence: Rithwick Rajagopal, MD, PhD, 660 S Euclid Ave, St. Louis, MO 63110 (email: rajagopalr@wustl.edu).*



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