Effects of Green Diode Laser in the Treatment of Pediatric Coats Disease

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• PURPOSE: To review the effect of green diode laser ablation therapy on retinal structure and functional outcome in patients with advanced Coats disease.
• DESIGN: Retrospective, interventional case series.
• METHODS: Fourteen eyes of 13 patients with Coats disease were included in this study. Medical records, Retcam photographs (Clarity Medical Systems, Pleasanton, CA), and fluorescein angiograms were reviewed. All patients initially were treated with green diode laser (532 nm) ablation therapy to areas of the retinal telangiectasis associated with exudation. Main outcome measures included visual acuity, treatment outcome defined as complete resolution of telangiectatic lesions or exudative detachment, and macular status at the end of follow-up.
• RESULTS: Before treatment, 1 eye was at stage 2 (telangiectasis and exudation), 12 eyes were at stage 3 (exudative retinal detachment), and 1 eye was at stage 4 (total retinal detachment with glaucoma). Five eyes had highly detached retina of more than 4 mm. Median age at diagnosis was 51 months (range, 0.5 to 153 months). Median follow-up was 39.5 months (range, 15 to 70 months). Median number of green diode laser photocoagulation treatments was 2 (range, 1 to 5). After laser photocoagulation, 13 (93%) of 14 eyes had no active exudation. Functionally, 4 (29%) of 14 eyes had 20/50 or better visual acuity, 3 (21%) of 14 eyes had 20/60 to 20/200 visual acuity, 5 (36%) of 14 eyes had 20/400 to light perception visual acuity, and 2 (14%) of 14 eyes had no light perception visual acuity. No eye was phthisical or enucleated.
• CONCLUSIONS: Green diode laser therapy can be an effective treatment for advanced Coats disease, even in the presence of a moderate to severely elevated retinal detachment. (Am J Ophthalmol 2011;151:725–731. © 2011 by Elsevier Inc. All rights reserved.)

Accepted for publication Oct 15, 2010.

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COATS DISEASE IS AN IDIOPATHIC CONDITION characterized by vascular abnormalities of the retina that classically presents as telangiectatic and aneurysmal retinal vessels associated with subretinal and intraretinal exudation and often subtotal or total exudative retinal detachment.[1–8] The most common complication of Coats disease is progressive exudative retinal detachment.[9] Less common but severe complications include iris neovascularization, neovascular glaucoma, and anterior chamber cholesterolosis.[9] It typically is characterized by unilateral (approximately 80% of cases) retinal involvement in young males, with the disease being 3 times more prevalent in males than females.[10,11] No racial or ethnic association has been established.[10,11]

The current standard treatment is laser therapy for mild to moderate cases, and cryotherapy, surgical repair, or both for moderate to severe cases.[12] In the past, these treatments have been only somewhat successful in achieving structural improvement or disease resolution. In the largest study to date (n = 124 eyes) using laser, cryotherapy, and surgical repair, 76% of patients achieved structural improvement or stability.[12] Another recently published case series that used infrared laser therapy alone for all stages showed structural improvement in 82% of patients.[13] Herein, we report our experience in treating a consecutive series of patients with Coats disease using green diode laser therapy.

METHODS

PATIENTS DIAGNOSED WITH COATS DISEASE AND TREATED with laser from September 2002 through May 2008 at the University of Illinois Eye & Ear Infirmary Retinal Service were identified from a database. Patient age, gender, ethnicity, age at presentation, disease stage at presentation, number and dates of laser therapies, and final treatment and structural outcomes were recorded. All patients were diagnosed, managed, and treated by 1 physician (M.J.S.) at the University of Illinois Eye & Ear Infirmary. While the patients were under anesthesia, the green diode laser ablation therapy was directed to vascular abnormalities, including microaneurysms, macroaneurysms, telangiectatic vessels, and feeding and draining vessels in areas of the retinal exudation. The laser used was a 532-nanometer green diode laser (Iridex Corporation, Mountain View, CA). The specifics of the laser treatment in this study were

0002-9394/$36.00
doi:10.1016/j.ajo.2010.10.024

TABLE 1. Structural Staging Classification in Coats Disease

Stage	Description
0	Regressed; no telangiectasia/exudation
1	Retinal telangiectasia only
2	Telangiectasia and exudation
2A	Extra-foveal exudation
2B	Foveal exudation
3	Exudative retinal detachment
3A1	Extra-foveal detachment only
3A2	Foveal detachment
3B	Total retinal detachment
4	Total retinal detachment and glaucoma
5	Advanced end-stage disease

Classification based on Shields JA, et al.[12]

as follow: each treatment was performed using indirect ophthalmoscopy delivery and 28- and 20-diopter lenses. The console settings began at 200 mW, with a duration of 1000 ms. The interval was controlled by foot pedal and was cycled rapidly to produce a near continuous treatment. The power was titrated higher until vessel whitening was achieved, which generally occurred at 400 to 750 mW; however, in some cases, power as high as 1000 mW was needed. The higher settings were used for treating blood vessels in more highly elevated retina. Patients were followed up regularly with examination under anesthesia, and additional green diode laser ablative therapy was applied at each visit until a treatment end point was reached. The positive end point was complete resolution of the disease as defined by reattachment of the retina or resolution of exudation as evidenced by absence of leaking telangiectasis on fluorescein angiography, and the negative end point was continued exudation with laser treatment deemed to be providing no beneficial effects. Retcam (Clarity Medical Systems, Pleasanton, CA) photography and fluorescein angiography were performed for documentation, comparison, and staging purposes.

Structural assessment on presentation was based on the Coats staging classification previously described (Table 1).[9,12] The staging was carried out by 1 physician (M.P.B.) retrospectively based on Retcam photographs. Highly elevated retinal detachment was defined as that of more than 4 mm in elevation by ultrasound or indirect ophthalmoscopy. Macular status at final outcome was described as normal, macular atrophy, subretinal fibrosis, or tractional detachment by 2 physicians (M.J.S. and M.P.B.) based on Retcam photographs at final follow-up.

RESULTS

FOURTEEN EYES OF 13 PATIENTS WERE IDENTIFIED. TABLE 2 outlined the clinical characteristics of the patients in this study. Sixty-two percent of patients were male and 1 female patient had bilateral disease (eyes 1 and 12). Two female patients had Coats disease associated with extraocular syndromic elements. The median and mean age at diagnosis was 51 months and 57 months, respectively (range, 0.5 to 153 months). The median and mean length of follow-up was 39.5 months and 41 months, respectively (range, 15 to 70 months). The median and mean number of laser treatments applied to each patient was 2 and 2.4, respectively (range, 1 to 5). At diagnosis, 1 eye (7%) had extrafoveal exudation only (stage 2A), 8 eyes (57%) had foveal subtotal retinal detachment (stage 3A2), 4 eyes (29%) had total retinal detachments (stage 3B), and 1 eye (7%) had a total retinal detachment and glaucoma (Stage 4). Five (36%) of 14 eyes had a highly elevated retinal detachment. Figure shows representative cases in this series.

- **VISUAL OUTCOME:** Snellen visual acuity at final follow-up was as follows. Four (29%) of 14 eyes had 20/50 or better visual acuity, 3 (21%) of 14 eyes had 20/60 to 20/200 visual acuity, 5 (36%) of 14 eyes had 20/400 to light perception visual acuity, and 2 (14%) of 14 eyes had no light perception visual acuity. One patient with light perception vision (eye 11) had developmental delay precluding accurate visual acuity measurement.

- **TREATMENT END POINT:** Overall, 13 (93%) of 14 eyes reached a positive end point after laser treatments alone and had no active exudation after laser treatment. One patient (eye 14) failed laser treatment: the retina remained completely detached and required external subretinal fluid drainage and laser treatment. This eye eventually achieved complete absence of exudation.

- **STRUCTURAL OUTCOME:** In the macula, 3 eyes (21%) had normal foveal reflex, 3 eyes (21%) had mild atrophy, 3 eyes (21%) had moderate atrophy, 3 eyes (21%) had subretinal fibrosis, and 2 eyes (14%) had tractional detachment. Two eyes (14%) had intraocular pressure of more than 21 mm Hg. No child had orbital asymmetry or required a cosmetic ocular prosthetic. No eye was painful. In no eye did phthisis bulbi develop, nor was any eye enucleated.

- **TREATMENT COMPLICATIONS:** Untoward events thought to be related directly to laser treatment in this case series are listed in Table 2. In 1 eye, mild cataract developed, and in 2 eyes, significant cataract developed requiring vitrectomy and lensectomy after completion of laser treatment. All the cataracts occurred in patients with high retinal detachment. Vitreous hemorrhage or rhegmatogenous retinal detachment was not observed.

TABLE 2. Green Laser for Pediatrics Coats Disease: Patient Characteristics and Outcome

Eye	Gender	Ethnicity	Eye	Age at Dx	VA at Dx	Stage[a] at Dx	No. of Treatments	F/U Length (mo)	IOP at Final F/U	Treatment Endpoint	Functional Outcome (Final VA)	Structural Outcome	Complications
1	F	Caucasian	OS	1 y 5 mo	n/a	2A	2	43	21	No exudation	20/25	Normal	None
2	M	African Am	OD	0.5 mo	CF	3B	1	32	20	No exudation	20/200	Moderate atrophy	None
3	M	Caucasian	OD	12 y 6 mo	20/200	3A2	1	27	7	No exudation	20/50	Mild atrophy	None
4	M	Caucasian	OD	8 y 9 mo	20/40	3A2	3	54	14	No exudation	20/30	Normal	None
5	F	Caucasian	OS	3 y 8 mo	CF	3B	3	70	14	No exudation	20/400	Mild subfoveal fibrosis	None
6	M	African Am	OS	4 y 7 mo	CF	3A2	2	57	17	No exudation	CF	Moderate subfoveal fibrosis	None
7	M	Caucasian	OS	11 y 10 mo	20/60	3A2	3	15	14	No exudation	20/40	Normal	None
8	F	Hispanic	OD	12 y 9 mo	20/400	3A2	1	57	14	No exudation	20/200	Mild atrophy	None
9	M	Caucasian	OS	2 y 2 mo	n/a	3A2[b]	5	33	13	No exudation	NLP	Tractional detachment	None
10	M	Caucasian	OD	6 y 1 mo	CF	3A2[b]	3	36	8	No exudation	20/160	Moderate subfoveal fibrosis	None
11	F	African Am	OD	4 y 8 mo	No F/F	3A2	2	49	20	No exudation	LP[c]	Mild atrophy	None
12	F	Caucasian	OD	1 y 5 mo	n/a	3B[b]	2	43	21	No exudation	LP	Moderate atrophy	Cataract (mild)
13	F	Hispanic	OD	11 mo	n/a	3B[b]	2	31	28	No exudation	HM	Moderate atrophy	Cataract
14	M	Caucasian	OD	1 y 2 mo	n/a	4[b]	4	30	35	Persistent exudation	NLP	Tractional detachment	Cataract
Mean				4 y 9 mo			2.4	41					

Eye 1 and 12 are from the same patient who has bilateral disease.

CF = count fingers; Dx = diagnosis; F = female; F/U = follow up; HM = Hand motion; LP = Light perception; M = male; mo = month; n/a = not available; NLP = no light perception; RD = retinal detachment; y = year.

[a]Staging was based on previous published literature.[12] See Table 1.

[b]Indicates presence of highly elevated retinal detachment of >4 mm by ultrasound or indirect ophthalmoscopy.

[c]Patient has developmental delay.

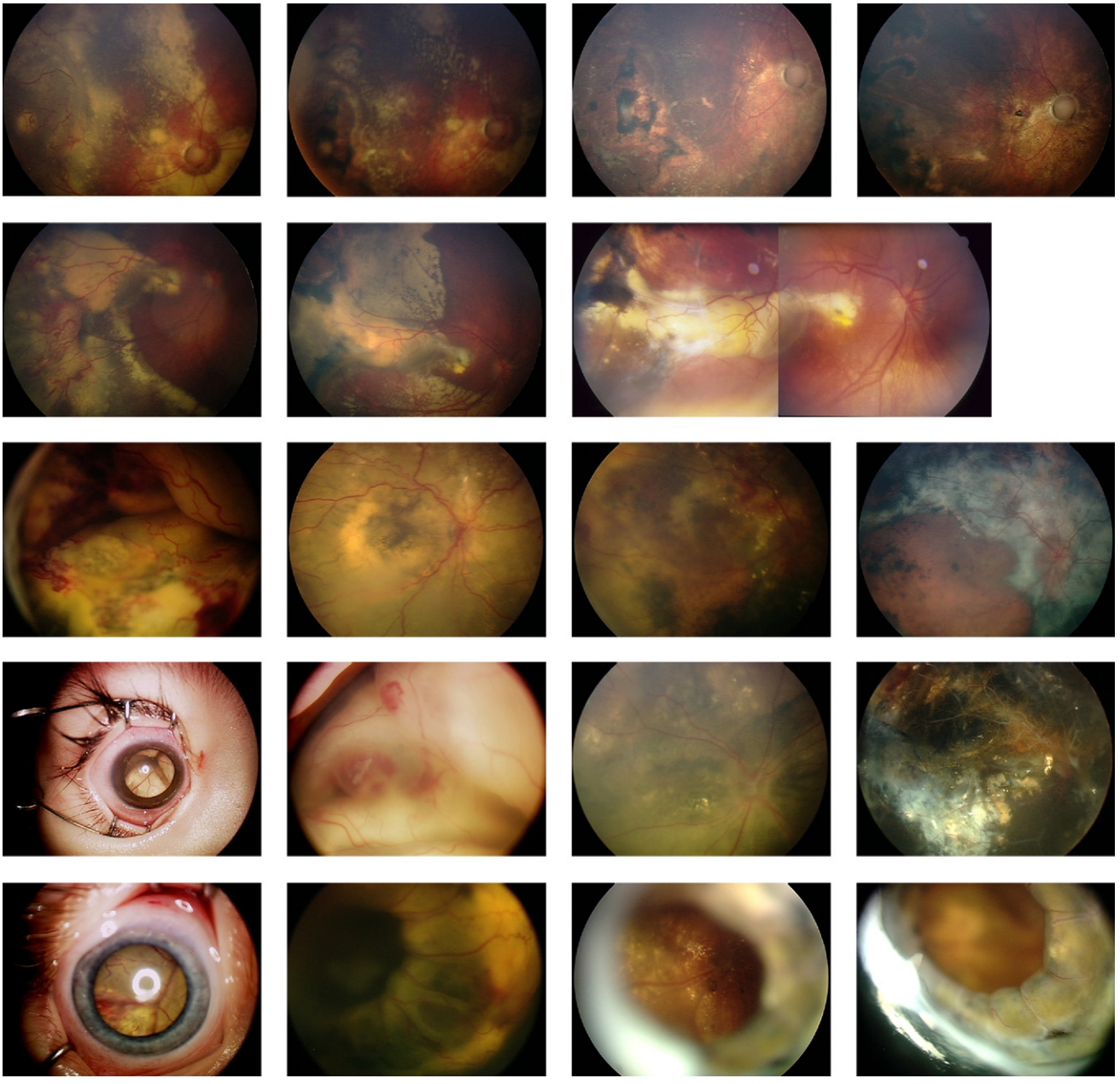

FIGURE. Images from representative cases demonstrating effects of green laser photocoagulation in advanced Coats disease. (Top row far left) Eye 11 at diagnosis showing exudation involving the fovea and retinal detachment temporally. (Top row near Left) Two months after treatment with residual exudation and elevation. (Top row near right) Ten months after initial treatment with residual exudation but no elevation. Second laser treatment was applied at this visit. (Top row far right) Seventeen months after initial treatment showing complete resolution of exudation and elevation. Visual acuity was at least light perception (patient had developmental delay precluding Snellen testing). (Second row far left) Eye 10 at diagnosis showing exudation involving the fovea and highly elevated exudative detachment temporally. Laser was applied at diagnosis and at 2 months. (Second row near left) Four months after initial treatment with improvement of elevation but residual exudation remaining. (Second row near and far right) Fourteen months after treatment with no active exudation. Moderate subretinal fibrosis in the macula was present. Visual acuity was 20/160. (Third row far left) Eye 12 at diagnosis showing total retinal detachment with massive exudation and telangectatic vessels. Laser was applied at diagnosis and at 2 months. (Third row near left) Three months and (Third row near right) 8 months after initial treatment showing marked improvement, although residual exudation and retinal elevation remain. (Third row far right) Thirty-four months after initial treatment showing no residual exudation or retinal elevation. There was moderate atrophy of the macula, and visual acuity was light perception. (Fourth row far left) Eye 13 at diagnosis showing total retinal detachment behind the lens precluding view of optic nerve. Patient initially was referred for enucleation. Laser was applied at diagnosis and (Fourth row near left) at 2 months. (Fourth row near right) Four months after initial treatment showing marked improvement of elevation;

DISCUSSION

OUR DATA DEMONSTRATE A FAVORABLE STRUCTURAL response after green laser treatment for advanced Coats disease even in the presence of highly elevated retinal detachment, with 93% showing no exudation after laser treatment alone.

There have been several published reports of treatment of Coats disease in the literature.[13–23] Most of these studies consist of multimethod treatment regimens, using observation, laser, cryotherapy, surgical management, and enucleation. In the most extensive case series published to date, Shields and associates reviewed 124 eyes with Coats disease treated with the above methods.[12] They reported structural improvement in 48% of their patients, stability in 28%, worsening in 8%, and enucleation in 16%. However, laser photocoagulation therapy was used only when there was exudation but no retinal detachment or a very shallow detachment. Furthermore, cryotherapy was the treatment of choice in the presence of retinal detachment in that series. Reluctance to treat advanced Coats disease with laser may be based on the observation that the detached retina shows very poor absorption of laser treatment because energy generally is absorbed by the retinal pigment epithelium and heat then is transferred to the neural retina. However, in this series, we found that patients with Coats disease can be treated effectively with photocoagulation when it is directed at vascular abnormalities. The effect is the result of absorption by hemoglobin of green wavelength energy, which occurs even in the presence of highly elevated retinal detachment, where the neural retina is far from the retinal pigment epithelium.

Schefler and associates published the results of single-method treatment of Coats disease with infrared laser photocoagulation therapy.[13] Seventeen patients with Coats disease, with 14 patients having stage 3 disease or worse, were studied. Multiple treatments with an 810-nm infrared laser were used. In their study, 14 (82%) of 17 eyes showed improvement, 1 (6%) of 17 eyes remained stable, 2 (12%) of 17 eyes worsened, and 1 (6%) of 17 eyes required enucleation. In comparison, our study consisted of 14 eyes with 13 eyes having stage 3 disease or worse and 5 eyes having highly elevated retinal detachment. Overall, 13 eyes (93%) showed improvement, 1 eye (7%) remained stable, and none required enucleation. These data essentially are complimentary and add evidence to support the hypothesis that laser is an effective treatment method for this morbid condition.

In our study, of the 5 eyes with highly elevated detachment, 4 (80%) eyes achieved a positive treatment end point, whereas 1 eye failed treatment and required subretinal drainage. It is important to note that 2 of these 5 severe cases initially were referred for enucleation. Although there were significant subretinal fibrosis and atrophy in the macula, 3 eyes ended with some vision and none resulted in phthisis or poor cosmetic outcome. It is not clear how many eyes in the series by Schefler and associates had highly elevated detachment.

An important difference between studies, however, is that Schefler and associates used an 810-nm infrared laser for their treatments, whereas in our case series, we used a 532-nm green diode laser. The significance in difference between these 2 wavelengths is that hemoglobin absorbs green light more readily than the infrared spectrum.[22,24] Because of the greater absorption of hemoglobin in telangiectatic vessels, green 532-nm laser may be more effective for photocoagulative closure of vessel walls and aneurysms. Despite the difference in wavelength, the results of the studies are similar and a greater number of patients or more standard classification would be required to demonstrate statistical differences between treatments.

Mrejen and associates reported the use of green laser as a primary treatment of partial and total retinal detachment in 7 of their 15 Coats disease patients.[23] Anatomic success was achieved in 4 of 7 patients. The intervention protocol in that study was based on the surgeon's discretion, and 8 cases underwent primary cryotherapy and vitreoretinal surgery, whereas we used green laser as a primary treatment for all patients presented in this series. It is unclear how many eyes had highly elevated detachment, and the follow-up was somewhat limited in the laser-treated eyes. Although the differences in age, treatment protocol, outcome definition, and follow-up period preclude direct comparisons between our studies, we find it encouraging that there is 1 figure showing success in a 9-month-old patient with highly elevated detachment treated with green laser photocoagulation alone.

In addition to closure of aneurysms and vessel walls to impede leakage, an alternative mechanism of action of laser treatment in this disease may be decreased vascular endothelial growth factor (VEGF) production after retinal ablation.[13] Recently, several case reports have been pub-

the optic disc is visible. (Fourth row far right) Twenty-six months after initial treatment showing no active exudation but moderate macular atrophy with subretinal fibrosis and sclerotic vessels. Visual acuity was hand movements. (Fifth row far left) Eye 14 at diagnosis showing total retinal detachment behind the lens with elevated intraocular pressure. Laser treatment failed to improve exudation 1 month after treatment, and the patient underwent subretinal drainage. (Fifth row near left) Two months after drainage showing flattened posterior pole but total tractional retinal detachment anteriorly 360 degrees. A cataract developed and pars plana vitrectomy and lensectomy was performed at 6 months. (Fifth row near right and far right) Twenty months after diagnosis showing total retinal detachment in a so-called napkin-ring configuration with severe anterior fibrosis causing tractional detachment. Vision was no light perception, and further surgery to flatten the retina was deferred to prevent ciliary body damage and phthisis.

lished that have used VEGF inhibitors to treat Coats disease. Sun and associates reported elevated VEGF in an affected eye with Coats disease and demonstrated a reduction after an injection of pegaptanib.[25] Venkatesh and associates reported the use of intravitreal bevacizumab as primary treatment of Coats disease in 2 patients.[26] They reported that 1 patient improved from hand movements to 20/800, whereas the other patient remained stable 6 weeks after treatment. Laser then was applied and vision was stable after 1 year of follow-up in both patients. Cakir and associates reported stabilization after intravitreal bevacizumab and triamcinolone in an eye with stage 3A Coats disease after poor response to laser treatment.[27] There are also a few case reports of using intravitreal bevacizumab followed by laser treatment with improvement at up to 1 year of follow-up.[28–30] However, in cases where retinal detachment is highly elevated, it may be difficult or even impossible to administer intravitreal injections safely without injuring the retina. In such cases, it may be advantageous to use laser therapy first to attempt to flatten the retina before anti-VEGF treatment administration. If exudative detachment fails to respond, anti-VEGF can be considered at the time of subretinal fluid drainage. Further controlled studies using a greater number of patients followed up for many years will be needed to determine if intravitreal anti-VEGF agents have long-term benefits or complications when used in the pediatric population with newly diagnosed Coats disease.

Lens opacification has been reported in infants with retinopathy of prematurity as a complication of argon and diode laser photocoagulation at various wavelengths.[31–33] The exact mechanism is unknown, but theories include laser photocoagulation-induced uveal effusion leading to shallowing of the anterior chamber and subsequent corneal–lenticular touch[32] or the result of thermal injury of the lens caused by absorption and scattering of laser energy at the iris border, in vessels of the persistent pupillary membrane, or in the nucleus.[34] The 3 cataracts in our study were likely the result of increased energy required or proximity of the laser application to the lens resulting from marked elevation of the retina, because they occurred in the most advanced cases. We did not observe anterior chamber shallowing after laser treatment.

In the previously published literature on this subject, there has been no suggestion of ethnic association with Coats disease.[10] However, in our study we noted that of the 8 white patients, 6 (75%) were of Eastern European descent. Although the low number of eyes and lack of controlled comparison preclude statistical significance, we believe that this finding may warrant further investigation.

The limitations of our study include its retrospective study design and the relatively small sample size. Importantly, the staging classification across studies may not be uniform. Optical coherence tomography studies in diabetic retinopathy have shown that the range of microvascular leakage into the retina extends from severe exudative edema to exudative detachment. Therefore, using photography and ophthalmoscopy alone to differentiate severe stage 2 from mild stage 3 is unlikely to be uniform across observers. This makes comparison of different treatment protocols difficult to interpret. Redescription and reconsideration of the classification of Coats using newer imaging systems such as OCT may be helpful to allow a more uniform description of the cases and treatment outcomes across centers. Unfortunately, the present high costs of the imaging systems limit implementation of this advancement. Finally, to validate or compare this treatment method with other treatments, larger prospective studies with objective reading centers, randomization, and longer follow-up may be considered. However, given the rarity of this condition, larger prospective studies likely will prove challenging. Despite some limitations, this study provides evidence that Coats disease can be treated effectively with green diode laser photocoagulation even in the presence of significant retinal detachment.

PUBLICATION OF THIS ARTICLE WAS SUPPORTED BY AN UNRESTRICTED GRANT FROM RESEARCH TO PREVENT BLINDNESS, Inc, New York, New York. The authors indicate no financial conflict of interest. Involved in Design and conduct of the study (M.J.S., C.C.C., P.A.K., M.P.B.); collection (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.), management (M.J.S., C.C.C., P.A.K., M.P.B.), analysis (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.), and interpretation (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.) of data; and preparation (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.), review (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.), and approval (M.J.S., C.C.C., P.A.K., D.F.K., M.P.B.) of the manuscript. The University of Illinois-Chicago Institutional Review Board approved the research.

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Biosketch

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Biosketch

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