

Targeted Multimodality Treatment to Eliminate the Need for Enucleation in Advanced Coats Disease

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Abstract

Purpose: To examine the trends and outcomes in the management of Coats disease and evaluate the effects of a staged therapeutic approach using transpupillary laser vascular ablation, intravitreal (IVT) bevacizumab, and adjunct as-needed posterior sub-Tenon triamcinolone acetonide (used only in cases with a persistent active exudation) on globe retention, anatomic status, and visual acuity (VA). **Methods:** An evaluation was performed from 2005 to 2023. Previous case series published in the literature were reviewed. In total, the case series comprised 68 patients who were evaluated and treated. In addition, a retrospective consecutive chart review was performed of novel cases of children with advanced Coats disease (stage 3 and 4) who were treated with targeted laser ablation coupled with IVT bevacizumab injection and supplemented with as-needed posterior sub-Tenon triamcinolone acetonide. **Results:** All patients had total resolution of the retinal detachment, and no patient had evidence of neovascular glaucoma after treatment. At 24 months, 11 (42%) of 26 eyes had better than 20/50 VA, 10 (39%) of 26 eyes had better than 20/400 VA, and 5 (19%) of 26 eyes had better than 5/200 VA. No eye required enucleation or developed endophthalmitis or inflammation after therapy with IVT bevacizumab. In addition, no case required incisional surgery. **Conclusions:** Treatment trends for advanced Coats disease have evolved, leading to enhanced patient outcomes and improved quality of life. Combined treatment with IVT bevacizumab, transpupillary laser vascular ablation, and as-needed posterior sub-Tenon triamcinolone acetonide results in improved anatomic outcomes.

Keywords

Coats disease, intravitreal bevacizumab, targeted laser ablation, triamcinolone acetonide

Introduction

Coats disease is an idiopathic unilateral retinal vascular disorder that most commonly presents in men and is characterized by retinal telangiectasias, subretinal/intraretinal exudation, exudative retinal detachment (RD), secondary angioma, secondary glaucoma, or a combination.^{1,2} The exudative changes in Coats disease result from leakage of lipoproteic fluid from telangiectatic retinal vessels, which have a decreased number of endothelial cells.³ The most important differential to consider when diagnosing children is retinoblastoma, in particular because a Coats-like reaction may develop in some patients.

After studies showed that intravitreal (IVT) vascular endothelial growth factor (VEGF) levels are increased in patients with Coats disease,^{4,5} the approach to its treatment evolved considerably. Previous studies have shown positive outcomes in advanced Coats disease with combined IVT anti-VEGF agents and transpupillary laser vascular ablation.^{6,7}

The purpose of this single-surgeon study was to review the trends and outcomes in the treatment of Coats disease between 2005 and 2023^{6,8–10} and to evaluate how a staged therapeutic

approach using transpupillary laser vascular ablation, IVT bevacizumab, and adjunct posterior sub-Tenon triamcinolone acetonide treatment affects globe retention, anatomic status, and visual acuity (VA).

Methods

A retrospective consecutive chart review was performed of a cohort of novel cases of children with advanced Coats disease. Treatment consisted of targeted laser ablation (Iridex 810 nm laser indirect ophthalmoscope, large spot size, targeting only vascular abnormalities) coupled with IVT bevacizumab injection (Avastin)

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Table 1. Treatment Modality for Coats Disease and Outcomes Over 2 Decades.

Study ^a	Patients (n)	Treatment Modality ^b	Outcomes
Couvillion ⁸	1	Three sessions of large-spot diode laser	At 2 months, the exudative RD had resolved and the telangiectasia dimensions and involution of the retinal macrocyst had reduced.
Scheffler ⁹	17	Repetitive diode laser ablation (mean, 5)	94% rate of globe salvage (only 1 patient required enucleation); 82% of patients had complete resolution of telangiectasias and exudative RDs.
Villegas ⁶	24	Large-spot diode laser (mean, 7.4) and IVT bevacizumab injection (mean, 4.6)	100% of the patients had resolution of exudative RD, ablation of vascular telangiectasia, and anatomic improvement of the retina. No patient required enucleation.
Sein ¹⁰	26	810 nm diode laser (mean, 5.58), IVT bevacizumab injection (mean, 4.7), and sub-Tenon triamcinolone acetonide injections (mean, 2)	100% of patients had a reduction in vascular leakage and resolution of peripheral telangiectasias and RDs. No patient required enucleation.

Abbreviations: IVT, intravitreal; RD, retinal detachment.

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^bNote the shift from targeted laser to laser and antivascular endothelial growth factor to laser, antivascular endothelial growth factor, and as-needed posterior sub-Tenon triamcinolone acetonide.

at 1.25 mg/0.05 mL and supplemented with as-needed posterior sub-Tenon triamcinolone acetonide (40 mg/mL). An institutional review board (Larkin Community Hospital) approved the study, which was performed in accordance with the tenets of the Declaration of Helsinki and all applicable US Health Insurance Portability and Accountability Act of 1996 regulations.

The inclusion criterion was children with Coats disease (stage 3 or 4). Children with secondary exudative reactions or stage 1, 2, or 5 Coats disease were excluded. Ocular imaging studies were performed to evaluate patients and included intra-operative spectral-domain optical coherence tomography (OCT), widefield fluorescein angiography (FA)/fundus photography, and an A/B ultrasonography scan performed every 4 to 8 weeks. The RetCam (Natus) was used for widefield imaging and FA, while the Spectralis device (Heidelberg) or Silverstone device (Optos) was used for OCT. FA helped diagnose vascular anomalies and ischemia, and OCT evaluated macular structures, including macular edema (ME).

All treatments aimed to eliminate abnormal vasculature and ME. Patients included in this study had stage 3 or 4 Coats disease. The Shields classification system was used. Stage 3 Coats disease consisted of patients with exudative RD. Stage 3 was subdivided into type A (subtotal detachment) and type B (total detachment). Patients with stage 4 Coats disease had total RD and glaucoma. Standardized informed consent was obtained in all patients because off-label IVT bevacizumab was used. In addition, a review was performed of previously published case series with the purpose of evaluating the treatment trends of Coats disease over the past decades.

Results

This consecutive chart review comprised 26 patients with Coats disease (stage 3, 22 patients; stage 4, 4 patients). The mean age

at presentation of the 19 girls and 7 boys was 19 months (range, 21 days–48 months). All patients received a total of 129 injections of IVT bevacizumab (mean, 4.6 injections per patient; range, 2–9). All 26 patients also had a total of 156 laser diode treatment sessions (mean, 5.7 laser sessions per patient; range, 3–15). Of the 26 patients, 5 received 12 posterior sub-Tenon triamcinolone acetonide injections (mean, 1.8 injections per patient; range, 1–3). The endpoint for IVT/periocular therapy and laser treatment was resolution of active exudation and vascular activity. Patients were followed for a mean of 49.4 months (range, 18–84).

After treatment, all patients had total resolution of the RD and no patient had evidence of neovascular glaucoma (NVG). No eye required enucleation. No patient developed endophthalmitis or inflammation after IVT therapy with bevacizumab. At 24 months, 11 (42%) of 26 eyes had better than 20/50 VA, 10 (39%) had better than 20/400 VA, and 5 (19%) had better than 5/200 VA.

The review of previous cases focusing on the treatment trends of Coats disease comprised 68 patients who were evaluated and received treatment. Table 1 shows the results of this review. In a report by Couvillion et al,⁸ a 9-year-old patient received 3 laser sessions; by 2 months, the exudative RD had resolved and the telangiectasia dimensions and involution of the retinal microcyst had reduced. Scheffler et al⁹ implemented the use of repetitive diode laser ablation and achieved a 6% enucleation rate. In 2014, Villegas et al⁶ reported 100% resolution of exudative RDs and 0% enucleation rates with the use of a large-spot diode laser and IVT bevacizumab. Sein et al¹⁰ also found that incorporating the use of sub-Tenon triamcinolone acetonide with laser and IVT bevacizumab resulted in 100% resolution of RDs and 0% enucleation rates. Of note is the shift from laser to laser and anti-VEGF to laser, anti-VEGF, and as-needed sub-Tenon triamcinolone acetonide (Figures 1–4).

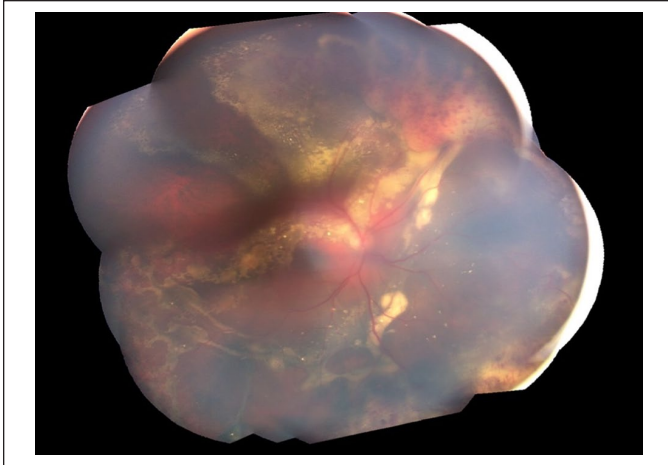


Figure 1. Color fundus montage photograph shows total exudative retinal detachment and Coats disease.

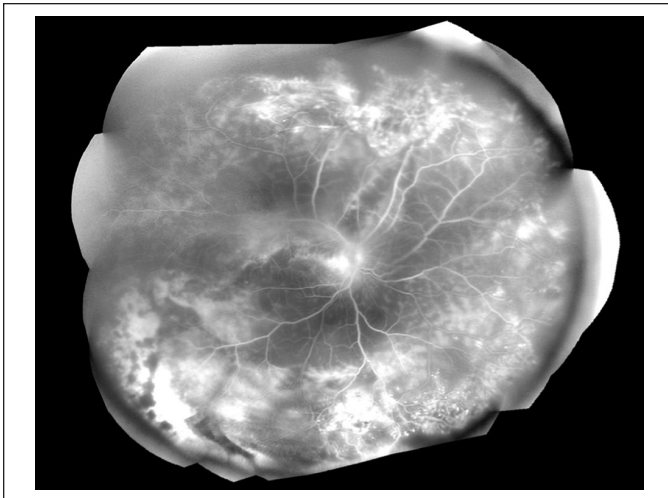


Figure 2. Montage fluorescein angiography shows retinal telangiectasias and aneurysmal dilations.

Conclusions

The management of Coats disease has advanced throughout the years. A recent study by Shields et al¹¹ evaluated the features and outcomes of Coats disease over 5 decades. In the 1970s, they found that approximately 39% of patients were only observed and 0% were treated with anti-VEGF. Eyes with Coats disease often required enucleation in the 1970s and 1980s; at the time, it was believed that application of a laser to a detached retina could bring about the formation of a retinal hole. More recently, there has been a shift to more widespread use of laser photocoagulation, sub-Tenon corticosteroids, and IVT anti-VEGF medications. The authors of this study proposed that the implementation of these medications contributed to improved resolution of subretinal fluid (SRF) and a reduced need for enucleation. A study in 2001 by Shields et al² reported that the enucleation rate was

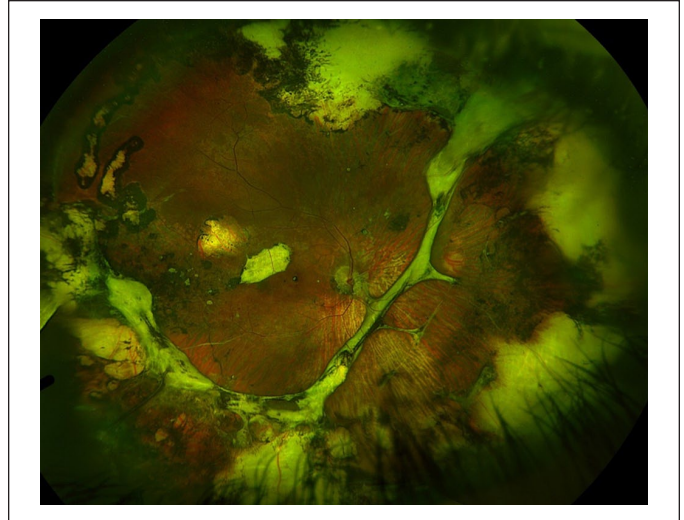


Figure 3. Extended follow-up at 62 months shows resolution of the retinal detachment with associated subretinal fibrotic changes in areas of previous exudation.

16%, mainly as a result of elevated intraocular pressure and iris neovascularization.

Laser photocoagulation, which directly targets abnormal retinal vessels, has been the most effective treatment in early stages of the disease. When lesions involve the periphery, cryotherapy may be implemented.¹² In a report by Scheffler et al,⁹ 17 patients with Coats disease were evaluated and treated with repetitive diode laser ablation. Eighty-two percent of the patients had complete resolution of telangiectasias and exudative RDs; only 1 patient required enucleation because of pain in a blind eye.

Although the pathophysiology of Coats disease has not been completely elucidated, studies have shown that VEGF plays an important role in disease progression. According to a study by Zhao et al,¹³ the IVT levels of VEGF are positively correlated with the extent of RD in patients with Coats disease. Anti-VEGF agents help regress abnormal blood vessels and assist in the resolution of ME.¹ These findings have led to the use of anti-VEGF medications to treat eyes with this condition. In a case series by Villegas et al,⁶ 24 children presenting with exudative RD associated with advanced Coats disease were treated with a large-spot diode laser and IVT bevacizumab injections. This therapeutic approach led to the resolution of RD in all cases.

Triamcinolone acetonide has been used in a wide variety of ocular conditions affecting retinal vascularity, such as diabetic retinopathy.¹⁴ Several studies have reviewed its effectiveness in the management of Coats disease. Alsakran et al¹⁴ performed a retrospective review of patients with Coats disease (stage 3 or higher) who received IVT triamcinolone acetonide. Complete resolution of SRF occurred in 76.4% of the patients after a mean of 1.3 injections and a mean of 2 laser sessions, and no surgical drainage was required. Jarin et al¹⁵ observed an improvement in ME in a 74-year-old man with Coats disease after the administration of IVT triamcinolone acetonide. However, the VA did not

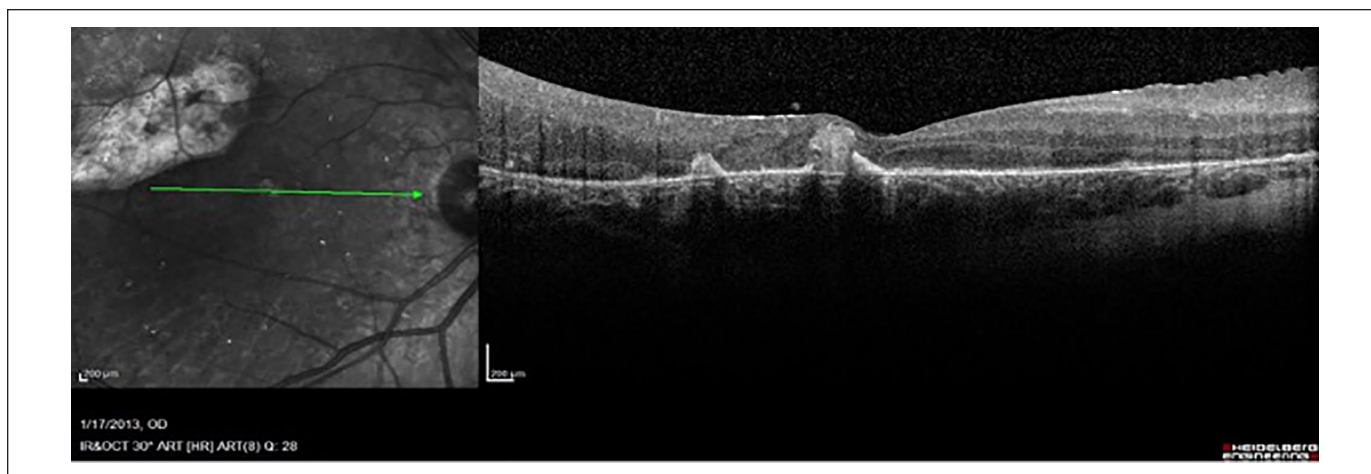


Figure 4. Macular spectral-domain optical coherence tomography shows secondary atrophic changes without evidence of active exudation at 62 months of follow-up.

improve in this patient during the follow-up. Sein et al¹⁰ evaluated 26 patients with Coats disease, implementing combination treatment with laser photocoagulation, IVT bevacizumab, and sub-Tenon triamcinolone acetonide. All patients had a reduction in vascular leakage and resolution of peripheral telangiectasias and RDs. No patient required enucleation.

In our current study, multimodality treatment with transpupillary laser vascular ablation (all 26 eyes), IVT bevacizumab (all 26 eyes), and adjunct posterior sub-Tenon triamcinolone (5 eyes) led to preservation of the eye and complete resolution of RD in all 26 patients. Current guidelines for this staged therapeutic approach consist of repetitive treatment with targeted laser and anti-VEGF administration. Posterior sub-Tenon triamcinolone acetonide is administered in cases that have persistent vascular activity after a minimum of 4 focal repetitive treatments with laser and anti-VEGF. Laser treatment was FA-guided in all cases, and all eyes achieved a VA better than no light perception. The worst VA was 5/200, and the best was 20/20. Furthermore, no eye developed NVG. Preventing the development of NVG in patients with Coats disease is critical because this progression typically leads to enucleation.² Possible complications of enucleation include exposure of the implant, orbital pain, pyogenic granulomas, and ptosis.¹⁶

Since 2005, there have been gradual changes in the management trends of Coats disease (Table 1). By that time, our team had transitioned from cryoablation to laser treatment. Several studies have reported patient outcomes with the use of cryotherapy. Egerer et al¹⁷ treated patients with photocoagulation or cryotherapy. Although most patients had resolution of the disease, recurrence rates were high. In addition, patients who had vascular involvement in 3 quadrants failed treatment. Bergstrom and Hubbard¹⁸ used combined IVT steroids and cryotherapy to treat patients with severe Coats disease and found a high rate of complications, including inoperable rhegmatogenous RDs and cataracts.

Limitations of this study include its retrospective nature, non-randomization, single surgeon, and small sample (26 patients).

There was also a lack of long-term follow-up and analysis of multimodal imaging patterns. Moreover, the simultaneous use of laser therapy may have complicated the assessment of the distinct effects of IVT/periocular therapy on the overall treatment success. In addition, the absence of a control group restricted our ability to draw conclusive findings regarding the optimal treatment approach.

We believe that the evolution in treatment trends of Coats disease over the years, from cryoablation to laser delivery and from single modality to combined modality with targeted laser, IVT anti-VEGF, and as-needed sub-Tenon triamcinolone acetonide, appears to have marked benefits in patient outcomes. The use of a combined modality helped avoid enucleation and, most important, enhanced patients' quality of life. Further studies are required to increase our knowledge regarding the management and outcomes of patients with Coats disease.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a US Health Insurance Portability and Accountability Act-compliant manner.

Statement of Informed Consent

Informed consent, including permission for publication of all photographs and images included herein, was obtained before the procedure was performed.

Declaration of Conflicting Interests

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