Predictors of enucleation in Coats disease: analysis of 259 eyes of 259 patients at a single center

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PURPOSE To evaluate the effects of clinical features associated with enucleation in eyes with Coats disease.

METHODS The medical records of all patients with Coats disease at the Ocular Oncology, Wills Eye Hospital from November 1, 1973, to July 31, 2018, were reviewed retrospectively. The clinical features pertaining to need for ultimate enucleation and time to enucleation were compared.

RESULTS The records of 351 eyes were reviewed, of which 259 had follow-up at our center and 32 (12%) were managed with enucleation. Reasons for enucleation included neovascular glaucoma (n = 24 [75%]), possible tumor (6 [19%]), and phthisis bulbi (2 [6%]). Compared to nonenucleated eyes, enucleated eyes had more extensive clock hour involvement of telangiectasia ($P < 0.001$), light bulb aneurysms ($P < 0.001$), exudation ($P < 0.001$), and subretinal fluid ($P < 0.001$). On adjusted analysis by binomial logistic regression, variables predictive of enucleation included presence of iris neovascularization ($P = 0.01$), ultrasonographic retinal detachment ($P = 0.004$), open-funnel retinal detachment ($P = 0.04$), closed-funnel retinal detachment ($P = 0.01$), ultrasonographic elevation of subretinal fluid by millimeters ($P = 0.001$), and angiographic extent of light bulb aneurysms by clock hours ($P = 0.02$). By Kaplan-Meier analysis of 4-year cumulative risk of enucleation, risk factors for enucleation included presence of iris neovascularization (hazard ratio [HR] 31.0; $P < 0.001$), ultrasonographic retinal detachment (HR 56.2; $P < 0.001$), open-funnel retinal detachment (HR 2.7; $P = 0.01$), and closed-funnel retinal detachment (HR 4.5; $P < 0.001$).

CONCLUSIONS Clinical features that predict risk of and time to enucleation in eyes with Coats disease include iris neovascularization, ultrasonographic presence and millimeter-elevation of retinal detachment, and angiographic extent of light bulb aneurysms. (J AAPOS 2019;23: 266.e1-9)

Coats disease is a nonhereditary, unilateral retinal vascular disease characterized by telangiectatic vessels, vascular micro- and macroaneurysms ("light bulbs"), and intraretinal and subretinal exudation. Patients typically present with vision loss, strabismus, or xanthocoria.[1] A retrospective study of 150 consecutive patients with Coats disease revealed that the disease usually presents in males (76%) at a median age of 5 years, with midperipheral or peripheral retinal telangiectasia mainly in the temporal fundus.[2] In that analysis, visual outcomes of >20/50 were achieved in 14% of eyes, and factors predictive of poor visual outcome (<20/200) included posterior disease, diffuse or superior location of disease, presence of retinal macrocysts, and failed resolution of subretinal fluid.[3] Similar visual outcomes have been reported in other large series.[4,5]

The management of Coats disease is directed to eradicating leaking telangiectasia and aneurysms to enable resolution of subretinal fluid and exudation. Methods of treatment include laser photocoagulation, cryotherapy, intravitreal antivascular endothelial growth factor (anti-VEGF) or corticosteroid medications, vitreoretinal surgery, and occasionally enucleation. In most cases, the eye can be saved using conservative therapies; however, advanced disease with painful glaucoma or phthisis bulbi may require enucleation.[3,6] In a comprehensive series of 150 consecutive cases, enucleation was ultimately performed in 16% after failure of other treatment methods, for painful neovascular glaucoma, or, mostly, for stage 4 disease.[3] In this study, we review a larger cohort

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of 351 eyes with Coats disease, of which 259 were managed and followed by our team, to more thoroughly explore the frequency of enucleation and factors that predict the need for enucleation.

Subjects and Methods

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Wills Eye Hospital. Informed consent was obtained from all subjects or their respective parents or guardians on presentation to our Ocular Oncology Service.

The medical and photographic records of all patients diagnosed with Coats disease at the Ocular Oncology Service at Wills Eye Hospital from November 1, 1973, to July 31, 2018, were retrospectively reviewed. Patients with uncertain or alternative diagnoses were excluded. Of those with Coats disease, outcomes were identified and separated into two groups: those that required enucleation and those that were managed without enucleation. Patients with uncertain or alternative diagnoses of Coats disease and lack of follow-up with our service after the initial visit were excluded from the analysis. Patients who presented to us but chose enucleation locally were included only if sufficient documentation was available regarding the enucleation.

Collected information included demographics (age at presentation, race, sex, and disease laterality), presenting clinical features (visual acuity in Snellen for verbal patients, nonverbal visual acuity for younger patients, intraocular pressure (IOP) in mm Hg, xanthocoria, presence of iris, retinal, and optic disk neovascularization, extent of telangiectasia, light bulb aneurysms, and subretinal fluid in quadrants and clock hours), imaging features by fluorescein angiography during examination under anesthesia (extent of telangiectasia, light bulb aneurysms, and subretinal fluid in quadrants and clock hours), imaging features by ultrasonography during examination under anesthesia (retinal detachment, type of retinal detachment, presence of subretinal fluid, measurement of subretinal fluid elevation by calipers [mm], presence of exudation), and treatment modalities (argon laser photocoagulation, cryotherapy, intravitreal anti-VEGF, sub-Tenon's corticosteroid injection, intravitreal corticosteroid injection, or a combination of these modalities). Grading of clinical and imaging features at presentation was recorded in each patient chart by the treating senior ocular oncologist. Detailed fundus drawings were available for each patient, detailing clinical evaluation of telangiectasias, microaneurysms, exudation, and subretinal fluid.

Coats disease was classified as stage 1 (only retinal telangiectasias), stage 2A, (telangiectasia and extrafoveal exudation), stage 2B (telangiectasia and foveal exudation), stage 3A1 (subtotal extrafoveal exudative retinal detachment), stage 3A2 (subtotal exudative retinal detachment involving the fovea), stage 3B (total exudative retinal detachment), stage 4 (total detachment and secondary glaucoma), or stage 5 (advanced end-stage disease).[3] Previously treated patients who presented with partially or completely resolved disease were characterized as unknown for staging.

Data were tabulated in Microsoft Excel 2016 and analyzed using SPSS software (version 18 for Windows; SPSS Inc, Chicago, IL). Continuous variables are expressed as mean (median, range). Comparison between eyes that came to enucleation and those that did not was performed using sample t test for continuous variables and χ^2 or the Fisher exact tests for categorical variables. Binomial logistic regression determined factors predictive of enucleation after adjustment for potential confounders. Odds ratio (OR) is reported as OR (95% CI). Kaplan-Meier analysis was performed to calculate the 4-year cumulative risk of enucleation with various clinical features. Hazard ratio (HR) was calculated using Cox regression survival analysis.

Results

The records of 351 patients (351 eyes) were reviewed. A total of 259 eyes of 259 patients were managed at our service and followed by our team. Of these, 32 eyes of 32 patients (12%) required enucleation. Indications for enucleation included neovascular glaucoma in 24 (75%), concern for intraocular tumor in 6 (19%), and phthisis bulbi in 2 (6%) eyes. Mean time to enucleation from date of presentation was 19 months (median, 0; range, 0-184).

Demographic characteristics are presented in Table 1. A comparison of the two groups (enucleation vs no enucleation) revealed no significant differences in age, race, sex, laterality, or study eye ($P > 0.05$). Both groups showed predominantly male sex (24 [75%] vs 194 [85%]; $P = 0.13$) and white race (27 [84%] vs 160 [70%]; $P = 0.70$), with mean age at presentation of 7 and 12 years, respectively ($P = 0.11$). All patients presented with unilateral disease.

Clinical and imaging features are provided in Table 2. There were 93 eyes (26%) with incomplete multimodal imaging data who were not evaluated using ultrasonography or fluorescein angiography (FA) at presentation. FA was available for 167 eyes (65%), and ultrasonography was available in 166 (64%). Compared to nonenucleated eyes, enucleated eyes had significantly worse (verbal) visual acuity (<20/200) (15 [47%] vs 73 [32%]; $P = 0.001$), higher mean IOP (24 mm Hg vs 15 mm Hg; $P < 0.001$), presence of iris neovascularization (17 [53%] vs 3 [1%]; $P < 0.001$), presence of corneal edema (3 [9%] vs 0 [0%]; $P < 0.001$), greater stage of disease (stage 3B or greater in 30 [94%] vs 82 [36%]; $P < 0.001$), and greater mean clock hours of telangiectasia (8 vs 5; $P < 0.001$), light bulb aneurysms (8 vs 4; $P < 0.001$), exudation (10 vs 7; $P < 0.001$), and subretinal fluid (11 vs 6; $P < 0.001$). Enucleated eyes were more likely to present with total retinal detachment (26 [81%] vs 78 [34%]; $P < 0.001$]). See Figure 1 A-B. There was no difference in presence of neovascularization of the retina or optic disk.

Regarding FA features, enucleated eyes presented with greater amount of telangiectasia (8 vs 6 clock hours; $P = 0.004$) and light bulb aneurysms (8 clock hours vs 5 clock hours; $P < 0.001$). There was no FA difference in the extent of retinal nonperfusion (6 clock hours vs 5 clock hours; $P = 0.43$). See Figure 1C. Ultrasonography features showed that eyes that came to enucleation were more likely to present with retinal detachment (24 [92%] vs 71 [51%]; $P < 0.001$), specifically, open funnel retinal detachment (13

Table 1. Patient demographics

Demographic features	Enucleation n = 32 eyes in 32 patients[a]	No Enucleation n = 227 eyes in 227 patients[a]	*P* value	Total N = 259 eyes in 259 patients[a]
Mean age at presentation, years	7 [2; 0-69]	12 [6; 0-77]	0.11	11 [5; 0-77]
Sex				
Male	24 (75)	194 (85)	0.13	223 (83)
Female	8 (25)	33 (15)		47 (17)
Race				
White	27 (84)	160 (70)		187 (72)
African American	3 (9)	39 (17)		42 (16)
Asian	0 (0)	6 (3)	0.70	6 (2)
Hispanic	2 (6)	15 (7)		17 (7)
Middle Eastern	0 (0)	3 (1)		3 (1)
Indian	0 (0)	4 (2)		4 (2)
Laterality				
Unilateral	32 (100)	227 (100)	NA	259 (100)
Study eye				
Right	18 (56)	103 (45)	0.25	121 (47)
Left	14 (44)	124 (55)		138 (53)

[a]Percentages indicated in parentheses after number of eyes; median and range, in square brackets.

[50%] vs 37 [26%]; $P = 0.02$) or closed-funnel retinal detachment (6 [23%] vs 9 [6%]; $P = 0.01$), and greater elevation of subretinal fluid in millimeters (12 mm vs 3 mm; $P < 0.001$). See Figure 1D, Figure 2.

Treatment information is provided in Table 3. Of the 32 enucleated eyes, 17 (53%) had enucleation as a primary treatment. In 15 eyes, (47%) enucleation was performed after attempts at treatment, that is, as a secondary treatment. In 10 of these secondary treatments, (31%) following 2 or more prior treatments. Enucleated eyes were treated less often with medical or laser therapy (13 [41%] vs 211 [93%]; $P < 0.001$), specifically with argon laser photocoagulation (5 [38%] vs 121 [57%]; $P < 0.001$) and cryotherapy (9 [69%] vs 165 [78%]; $P < 0.001$). See Figure 3.

Results of binomial logistic regression are provided in Table 4. After adjusting for potential confounders, analysis revealed that predictors of enucleation included presence of iris neovascularization (OR 19.82 [1.88-209.49]; $P = 0.01$), ultrasonographic retinal detachment (OR 8.85 [1.98-39.51]; $P = 0.004$), open-funnel retinal detachment (OR 5.31 [1.00-28.08]; $P = 0.04$), closed-funnel retinal detachment (OR 4.37 [1.40-13.59]; $P = 0.01$), ultrasonographic elevation of subretinal fluid by millimeters (OR = 1.20 [1.07-1.33]; $P = 0.001$), and angiographic extent of light bulb aneurysms by clock hours (OR = 1.35 [1.05-1.72]; $P = 0.02$). Each 1 mm increase in subretinal fluid on ultrasonography increased the risk for enucleation by 20% (OR = 1.20), and each additional clock hour of light bulb aneurysms by angiography increased the risk by 35% (OR = 1.35).

Results of 4-year Kaplan-Meier analysis are shown in Table 5. Estimated risk of enucleation was higher with the presence of iris neovascularization (HR 31.0; $P < 0.001$), ultrasonographic retinal detachment (HR 56.2; $P < 0.001$), open funnel retinal detachment (HR 2.7; $P = 0.01$), and closed-funnel retinal detachment (HR 4.5; $P < 0.001$). See Figure 4.

Discussion

Several retrospective studies and case series have described the clinical features, management, and outcomes of Coats disease.[2,3,7-12] Treatment methods in these studies primarily included ablative techniques, such as cryotherapy or laser photocoagulation, intravitreal injections of anti-VEGF or steroids, or vitreoretinal surgery.[2,3,7-12] In most studies, the frequency of enucleation has ranged from 5% to 16% in advanced Coats disease that developed painful, neovascular glaucoma or failed other therapies.[3,7-12] In the series of 158 eyes by Shields and colleagues,[3] the three factors that predicted enucleation by multivariate analysis included iris heterochromia, iris neovascularization, and higher mean intraocular pressure. In the current study, 101 new eyes were added to the existing cohort, and the larger total cohort was analyzed using binomial logistic regression and Kaplan-Meier analysis. Although iris neovascularization remained a risk factor for enucleation, additional clinical features were evaluated and found to be risk factors, including extent of retinal detachment and angiographic extent of light bulb aneurysms.

Consistent with previous studies, our study showed that the 32 (12%) eyes that came to enucleation presented with far more advanced disease, including neovascular glaucoma, total retinal detachment, and greater telangiectatic vessels, light bulb aneurysms, and subretinal fluid. In fact, most of these children were referred to rule out retinoblastoma with total retinal detachment, thus weighing our data toward more advanced disease, with 30 of 32 (94%) of those enucleated having group 3B or above compared to 82 of 227 (36%) of those without enucleation. The features predictive of risk for enucleation and time to enucleation included features of iris neovascularization, total retinal detachment, more elevated retinal detachment, and more extensive angiographic evidence of aneurysms (Table 5).

Table 2. Clinical and imaging features at presentation

Clinical and imaging features	Enucleation, n = 32 eyes in 32 patients[a]	No enucleation, n = 227 eyes in 227 patients[a]	*P* value	Total N = 259 eyes in 259 patients[a]
VA, no. (%)				
Verbal				
≥20/40	0 (0)	39 (20)		39 (11)
20/40-20/200	1 (3)	45 (17)	0.001	46 (13)
<20/200	15 (47)	73 (32)		88 (25)
Nonverbal				
Fix and follow	0 (0)	14 (6)		14 (5)
Poor fix and follow	2 (6)	13 (6)	0.07	15 (6)
No fix and follow	14 (44)	40 (18)		54 (21)
Uncooperative	0 (0)	3 (1)		3 (1)
IOP, mm Hg, mean (median; range)	24 [18; 7-60]	15 [15; 6-40]	<0.001	16 [15; 6-60]
Anterior segment findings, no. (%)				
Xanthocoria	16 (50)	87 (38)	0.21	108 (42)
Iris neovascularization	17 (53)	3 (1)	<0.001	20 (8)
Corneal edema	3 (9)	0 (0)	<0.001	3 (1)
Phthisis	0 (0)	0 (0)	NA	0 (0)
Coats disease stage, no. (%)				
1	0 (0)	3 (1)		3 (1)
2A	0 (0)	17 (7)		17 (7)
2B	0 (0)	29 (13)		29 (11)
3A1	1 (3)	34 (15)		35 (14)
3A2	1 (3)	54 (24)	<0.001	55 (21)
3B	14 (44)	80 (35)		94 (36)
4	15 (47)	2 (1)		17 (7)
5	1 (3)	0 (0)		1 (0.3)
Unknown[b]	0 (0)	8 (4)		8 (3)
Telangiectasia				
Clock hours, mean (median; range)	8 [8; 0-12]	5 [5; 0-12]	<0.001	5 [5; 0-12]
Quadrants, no. (%)				
0	0 (0)	11 (5)		11 (4)
1	4 (13)	66 (29)		70 (27)
2	7 (22)	67 (30)	0.01	74 (29)
3	5 (16)	48 (21)		53 (20)
4	11 (34)	31 (14)		42 (16)
No view[c]	5 (16)	4 (2)		9 (3)
Light bulb aneurysms				
Clock hours, mean (median; range)	8 [8; 0-12]	4 [4; 0-12]	<0.001	5 [4; 0-12]
Quadrants, no. (%)				
0	1 (3)	24 (11)		25 (11)
1	4 (13)	75 (33)		79 (35)
2	7 (22)	70 (31)	0.002	77 (34)
3	5 (16)	30 (13)		35 (15)
4	10 (31)	24 (11)		34 (15)
No view[c]	5 (16)	4 (2)		9 (3)
Exudation				
Clock hours, mean (median, range)	10 [12; 1-12]	7 [6; 0-12]	<0.001	7 [7; 0-12]
Quadrants				
0	0 (0)	9 (4)		9 (3)
1	3 (9)	34 (15)		37 (14)
2	2 (6)	72 (32)	0.001	74 (29)
3	3 (9)	36 (16)		39 (15)
4	19 (59)	72 (32)		91 (35)
No view[c]	5 (13)	4 (2)		9 (35)
Subretinal fluid				
Clock hours, mean (median, range)	11 [12; 3-12]	6 [6; 0-12]	<0.001	7 [7; 0-12]
Quadrants				
0	0 (0)	34 (15)		34 (13)

(*Continued*)

Table 2. Clinical and imaging features at presentation (*Continued*)

Clinical and imaging features	Enucleation, n = 32 eyes in 32 patients[a]	No enucleation, n = 227 eyes in 227 patients[a]	*P* value	Total N = 259 eyes in 259 patients[a]
1	1 (3)	44 (19)		45 (17)
2	0 (0)	44 (19)	<0.001	44 (17)
3	2 (6)	23 (10)		25 (10)
4	26 (81)	78 (34)		104 (40)
No view[c]	3 (9)	4 (2)		7 (3)
Posterior segment findings				
Neovascularization of disk	1 (0.3)	1 (0.4)	0.21	2 (1)
Neovascularization of retina	1 (0.3)	4 (2)	0.45	5 (2)
No view of fundus[c]	3 (9)	4 (2)	0.05	7 (3)
FA[a]	n = 11	n = 156		N = 167
Telangiectasia clock hours Mean (median; mode)	8 [8; 5-12]	6 [5; 0-12]	0.004	6 [6; 0-12]
Light bulb aneurysm, clock hours, mean (median, mode)	8 [8; 5-12]	5 [4; 0-12]	<0.001	5 [5; 0-12]
Retinal nonperfusion, clock hours, mean (median; mode)	6 [6; 0-12]	5 [5, 0-12]	0.43	5 [5, 0-12]
Ultrasonography[c]	n = 26	n = 140		N = 166
Retinal detachment	24 (92)	71 (51)	<0.001	95 (57)
Partial	1 (4)	13 (9)	0.48	14 (8)
Total	4 (15)	12 (9)	0.47	16 (10)
Open funnel	13 (50)	37 (26)	0.02	50 (30)
Closed funnel	6 (23)	9 (6)	0.01	15 (9)
Subretinal exudate	25 (96)	127 (77)	0.36	152 (92)
Subretinal fluid elevation, mm, mean (median; mode)	12 (14; 0-19)	3 [1; 0-19]	<0.001	5 [2; 0-19]

FA, fluorescein angiography; *IOP*, intraocular pressure; *VA*, visual acuity.
[a]Percentages indicated in parentheses after number of eyes; median and range, in square brackets.
[b]Staging unknown for 8 eyes secondary to resolved disease at presentation (n = 4) and media opacities (n = 4).
[c]No view secondary to media opacities (cataract, total serous retinal detachment).

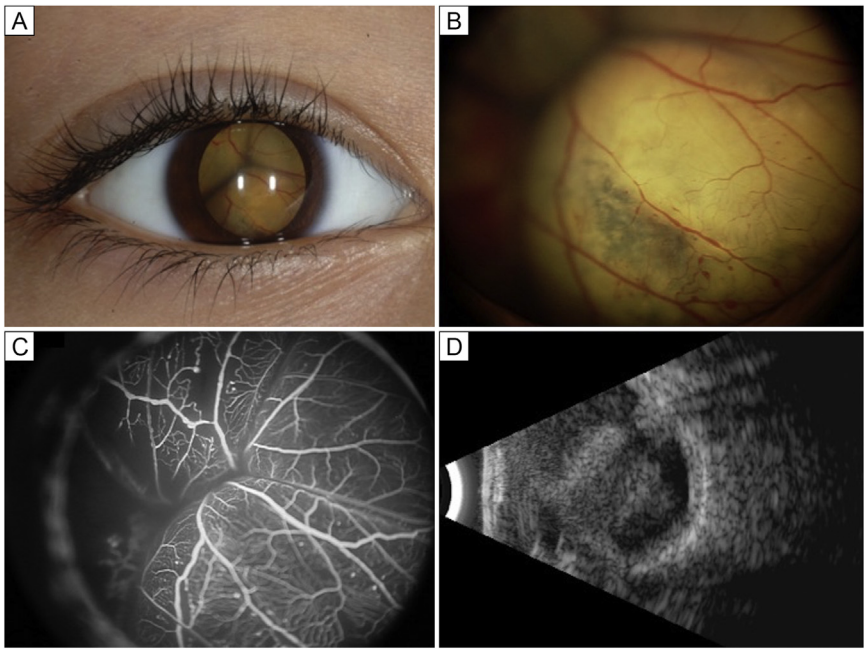

FIG 1. An 8-year-old boy with stage 4 Coats disease presented with total retinal detachment (A), exudative retinopathy with peripheral irregular telangiectasia and light bulb aneurysms, seen on fundus photography (B), confirmed on fluorescein angiography (C) and B-scan ultrasonography, which showed closed-funnel retinal detachment (D). The eye was enucleated for painful neovascular glaucoma and persistent retinal detachment.

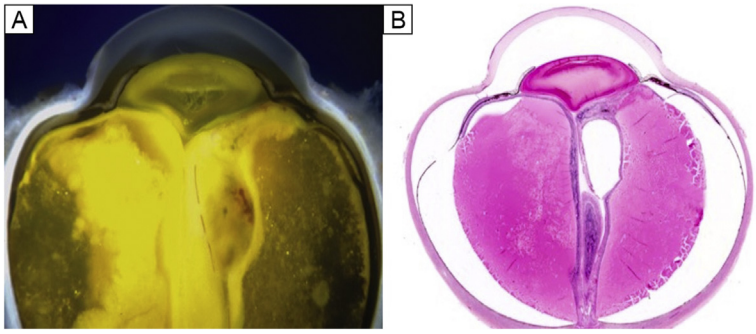

FIG 2. Pathology of Coats disease after enucleation. A, A 1-year-old boy with advanced Coats disease was primarily enucleated for painful neovascular glaucoma, showing the globe with total retinal detachment adherent to the posterior surface of the lens, anterior displacement of the lens, and extensive yellow subretinal exudation. B, On histopathology, dense proteinaceous fluid was in the subretinal space and thickened closed-funnel retinal detachment was noted. Further histopathology documented numerous cholesterol clefts and foamy histiocytes.

Table 3. Treatment modalities

Treatment	Enucleation, 32 eyes of 32 patients[a]	No enucleation, 227 eyes of 227 patients[a]	*P* value	Total, 259 eyes of 259 patients[a]
Primary enucleation	17 (53)		NA	17 (7)
Observation	2 (6)	16 (7)	0.58	18 (7)
Medical or laser therapy	13 (41)	211 (93)	<0.001	224 (86)
Total treatments, mean no. sessions	2.8 [2; 1-11]	3.9 [3; 1-26]	0.28	3.8 [3; 1-26]
	n = 13	n = 211		N = 224
Argon laser photocoagulation	5 (38)	121 (57)	<0.001	126 (56)
Mean no. sessions	1.6 [2; 1-2]	2.1 [1; 1-20]	0.58	2.1 [2; 1-20]
Cryotherapy	9 (69)	165 (78)	<0.001	174 (78)
Mean no. sessions	2.2 [1; 1-7]	2.2 [2; 1-9]	0.88	2.2 [2; 1-9]
Anti-VEGF injection	2 (15)	31 (15)	0.27	33 (15)
Mean no. injections	1.0 [1; 1-1]	3.7 [2; 1-20]	0.40	3.6 [2; 1-20]
Sub-Tenon's corticosteroid injection	2 (15)	33 (16)	0.19	35 (16)
Mean no. injections	1.0 [1; 1-1]	1.3 [1; 1-4]	0.53	1.3 [1; 1.0-4]
Intravitreal corticosteroid injection	3 (23)	9 (4)	0.38	12 (5)
Mean no. injections	1.3 [1; 1-2]	2.4 [1; 1-10]	0.54	2.2 [3; 1-10]

VEGF, vascular endothelial growth factor.
[a]Percentages indicated in parentheses after number of eyes; median and range, in square brackets.

Thus, earlier diagnosis and treatment at a time before these features develop could alleviate the risk for enucleation.

To prevent disease progression and decrease the risk of eventual enucleation, medical and laser therapy should be optimized. Although cryotherapy has traditionally been a common treatment for Coats disease with extensive exudation or subretinal fluid, recent studies have evaluated methods of control for highest-risk eyes demonstrating total retinal detachment using ablative, confluent external laser photocoagulation for direct eradication of leaking telangiectasia, as well as the use of intravitreal triamcinolone injection and the technique of nonvitrectomized drainage of subretinal fluid.[13-17] Levinson and Hubbard[15] evaluated 5 eyes with Coats disease and total retinal detachment managed with 577-nanometer yellow laser photocoagulation and found subretinal fluid resolution with an average of 2 sessions of laser photocoagulation, with 2 eyes (40%) achieving complete resolution of subretinal fluid after a single treatment session. Bergstrom and Hubbard[16] studied 5 eyes with total retinal detachment from Coats disease treated with intravitreal corticosteroid injection (4 mg/0.1 mL) delivered as a single dose followed by cryotherapy at 1-4 months and found reattachment of the retina in 2 (40%) eyes. Ghazi and colleagues[17] reviewed 4 cases of Coats disease with total retinal detachment managed with a single dose of intravitreal corticosteroid injection (1 mg/0.1 mL) and found partial to total resolution of subretinal fluid within 4 weeks for all 4 eyes, which allowed for further ablative therapy. Adjunct therapy with intravitreal anti-VEGF can potentially decrease vascular leakage, subretinal fluid, and exudation, but lack of scientific evidence and potential complications of vitreoretinal

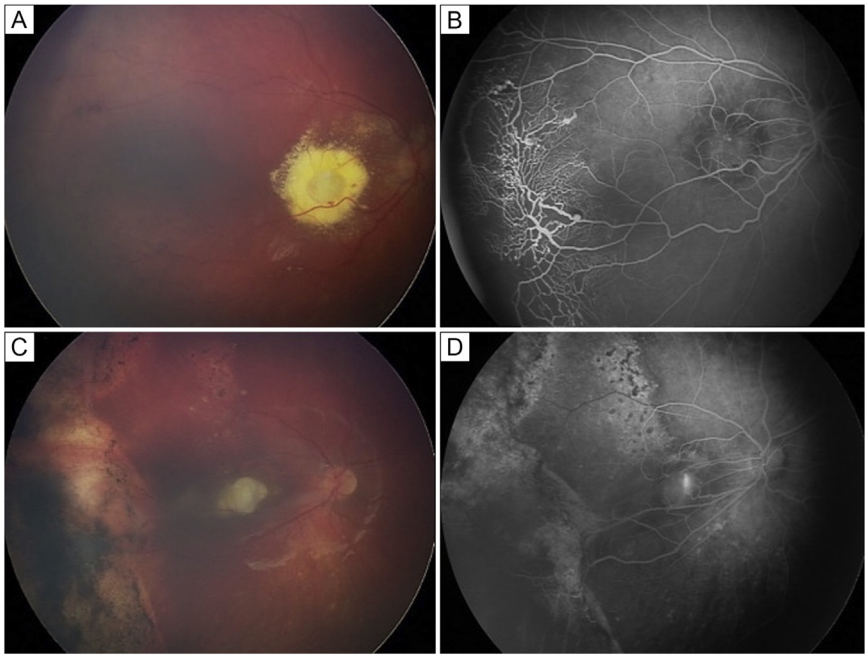

FIG 3. A 1-year-old girl with stage 2B Coats disease presented with foveal exudation and peripheral telangiectasia (A), confirmed on fluorescein angiography in the temporal periphery (B). On follow-up 24 months after argon laser photocoagulation and cryotherapy, telangiectasia and foveal exudation had resolved (C), leaving a gliotic macular scar, (D) confirmed on fluorescein angiography (D).

Table 4. Binomial regression analysis of variables predictive of enucleation

Predictive factors	OR	95% CI	*P* value
Age, years	0.99	0.98-1.01	0.31
VA, logMAR	1.02	0.34-3.03	0.98
IOP, mm Hg	1.09	0.86-1.39	0.47
Xanthocoria	4.15	0.52-33.15	0.18
Neovascularization of the iris	19.82	1.88-209.49	0.01
RD by USG	8.85	1.98-39.51	0.004
Open funnel RD by USG	5.31	1.00-28.08	0.04
Closed funnel RD by USG	4.37	1.40-13.59	0.01
Subretinal fluid, mm, by USG	1.20	1.07-1.33	0.001
Telangiectasias by FA, clock hours	0.73	0.31-1.72	0.47
Light bulb aneurysms by FA, clock hours	1.35	1.05-1.72	0.02
Nonperfusion by FA, clock hours	1.07	0.84-1.36	0.59

CI, confidence interval; *FA*, fluorescein angiography; *IOP*, intraocular pressure; *OR*, odds ratio; *VA*, visual acuity; *RD*, retinal detachment; *USG*, ultrasonography; *VEGF*, vascular endothelial growth factor.

Table 5. Four-year Kaplan-Meier analysis

Risk factor	Presence of risk factor	4-year cumulative percentage of enucleation	Hazard ratio	*P* value[a]
Iris neovascularization	Yes	85	31.0	<0.001
	No	6		
RD by USG	Yes	28	56.2	<0.001
	No	0		
Open-funnel RD by USG	Yes	29	2.7	0.01
	No	10		
Closed-funnel RD by USG	Yes	41	4.5	<0.001
	No	13		

RD, retinal detachment; *USG*, ultrasonography.
[a]Log-rank test.

traction and systemic adverse effects in children has limited its use.[11,18-21] Moreover, several small series report successful results of surgical drainage of total retinal detachment in Coats disease. Adam and colleagues[22] reviewed 6 eyes treated with posterior sclerotomy with drainage of subretinal fluid followed by cryotherapy, showing retinal reattachment in 3 (50%) eyes at 12-36 months. Stanga and colleagues[23] evaluated transcleral drainage of subretinal fluid followed by intravitreal anti-VEGF injection (1.25 mg/1 mL) in 8 eyes with extensive retinal detachment to find complete resolution of subretinal fluid after 1 session of drainage and 1-2 sessions of injection in all 8 (100%) eyes, allowing for further treatment with laser photocoagulation. Silodor and colleagues[24] studied 13 eyes treated with external drainage of subretinal fluid and cryotherapy and found that none (0%) developed neovascular glaucoma, indicating that combination therapy could be effective in patients with advanced disease. These newer surgical treatment modalities are underway with our team and potentially could reduce the need for enucleation in the future.

Our study was a retrospective analysis, with data collection from a single center with two surgeons (CLS and JLS). Additional study limitations include incomplete multimodal imaging data in 26% of patients, who were not evaluated using all types of imaging at presentation. Moreover, many eyes were referred to rule out retinoblastoma at our

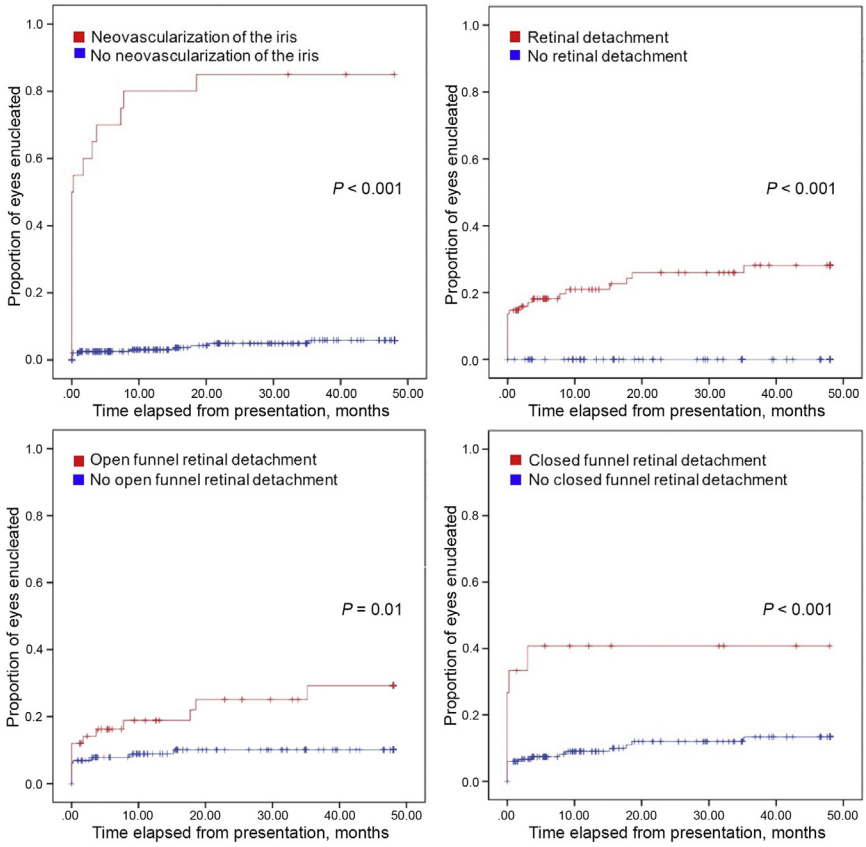

FIG 4. Kaplan Meier analysis of enucleation in Coats disease. Estimated 4-year risk for enucleation was higher with iris neovascularization (HR 31.0; $P < 0.001$), retinal detachment (HR 56.2; $P < 0.001$), open funnel retinal detachment (HR 2.7; $P = 0.01$), and closed-funnel retinal detachment (HR 4.5, $P < 0.001$).

ocular oncology center, reflecting the advanced stage of disease at presentation: 17 eyes were treated with primary enucleation, underscoring the skewed distribution of disease severity. Another limitation is the long period of data collection, extending over 4 decades. Over time, treatment philosophies have changed and imaging modalities have become more sophisticated. Thus, imaging data were acquired from several types of cameras. Wide-angle RetCam (RetCam; Natus Medical, Pleasanton, CA) imaging for fundus photography and fluorescein angiography became available in 1997 but was not used in older decades. Our data show fewer cases managed with enucleation in recent years over the 4 decades (1970s vs 1980s vs 1990s vs 2000s vs 2010s: 17% vs 27% vs 14% vs 13% vs 6%; $P = 0.04$).[25] Nevertheless, the large cohort reported in this study allowed for robust statistical analysis that was not previously possible with smaller reported series of Coats disease. Moreover, detailed and organized notes and fundus drawings allowed for thorough analysis of clinical characteristics and identification of clinical predictors for enucleation.

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