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Surgical & Medical Retina, Uveitis, Macular Degeneration & Diabetic Eye Disease

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RETINA DIGEST®

SPRING 2017

Retinal Detachment and Acute Retinal Necrosis

When vision loss occurs in a patient with acute retinal necrosis (ARN), retinal detachment (RD) is often the cause. Traditional ARN therapy includes the intravenous or oral administration of systemic antivirals. To determine the long-term visual and surgical outcomes of patients with RD associated with ARN, Kopplin et al from the Oregon Health & Science University evaluated the rates and risk factors for recurrent RD in 27 ARN patients (32 eyes) who underwent primary RD repair for ARN-related RD from 2001 to 2012 with ≥6 months follow-up. Patient records were examined for demographic data, visual acuity, development of RD or recurrent RD, surgical interventions and timing, viral polymerase chain reaction results, systemic antiviral and steroid treatment, and intravitreal foscarnet therapy.

Fifteen eyes in 13 patients developed RD; 13 eyes in 12 patients (average presenting age, 40.1 years; 53.8% men) required surgical repair. All patients received systemic antiviral treatment; 11 patients also received systemic prednisone. Pars plana vitrectomy (PPV) with silicone oil was performed in 53.8% of the cases. Recurrent RD developed in 6 eyes from 1 to 10 months after the primary retinal procedure, and repeat surgery was performed as needed.

The following visual outcomes were assessed for the 12 eyes that remained at the 1-year initial RD repair follow-up:

- 5 eyes demonstrated severe vision loss (Snellen visual acuity <20/200)
- 3 eyes had an initial macular-involving detachment

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- 3 eyes developed a recurrent RD (2 with prior macular detachment)
- 3 eyes (25%) had visual acuity better than 20/70

Visual acuity findings at the final follow-up were similar to those at 1 year. Recurrent RD was not always associated with poor visual outcomes.

Due to the rarity of ARN-related RD, the optimal approach for primary surgical repair remains challenging to assess. Reattachment in combination with silicone oil can be beneficial, but because recurrent RD after primary repair is a frequent complication of ARN, the long-term visual prognosis remains guarded.

Kopplin LJ, Thomas AS, Cramer S, et al. Long-term surgical outcomes of retinal detachment associated with acute retinal necrosis. Ophthalmic Surg Lasers Imaging Retina *2016;47:660-664.*

Long-term Visual Outcomes For Ocular Toxocariasis

Ocular toxocariasis (OT), a parasitic eye infection caused by ingesting food soiled by cat or dog feces containing *Toxocara cati* or *Toxocara canis* larvae, is typically associated with significant vision loss. The atypical features of this infection can misguide and/or delay diagnosis. To examine the clinical characteristics and treatment outcomes of proven OT in adult patients, Despreaux et al from Paris VI University, France, conducted a retrospective interventional case series of 14 patients (mean age, 45.6 years) diagnosed by positive serology and positive Western blot (WB) between June 2011 and November 2013.

Patient outcomes were assessed based on best-corrected visual acuity (BCVA), intraocular pressure, anterior or posterior segment inflammation, optical coherence tomography data including central foveal thickness (CFT; Figure 1), fluorescein angiography and indocyanine green angiography. Data collection occurred at baseline and final visit, with a 1-year follow-up period.

All patients received a systemic antihelminthic regimen of 200 mg of albendazole 2× daily for 15 days. Corticosteroid (CS) therapy was added if macular edema (ME) and/or posterior inflammatory reaction were present. Five patients underwent systemic CS therapy; 7 underwent local CS therapy. Vitrectomy was performed in 28.6% of the cases presenting with severe and persistent vitreous inflammation. In these eyes, CFT significantly decreased ($p = .017$) and mean BCVA significantly increased ($p = .01$; Table 1).

A higher incidence of ME in this study seemed to correlate with a delayed diagnosis (>8 months),

Table 1. Long-term visual outcomes of ocular toxocariasis in the adult: patients' clinical and ancillary findings at 1-year follow-up

	Baseline value	Baseline range	Value at 1-year follow-up	1-year follow-up range	*p* value
BCVA (Snellen)	20/100	20/800 to 20/25	20/63	20/400 to 20/20	.18
Anterior chamber inflammation flare (photons/ms)	41.1 ± 60.94	2–223	14.4 ± 14.1	2–59.4	.06
Posterior chamber inflammation[a]	1.7 ± 0.4	1–3	0.37 ± 0.4	0–1	<.001[b]
Central foveal thickness (μm)	402 ± 98.9	190–496	249.3 ± 36.4	187–310	.01[b]
Macular edema	10 (71.4)		1 (7.1)		<.001[b]
Active granuloma	11 (78.6)		0 (0)		<.001[b]
Epiretinal membrane	5 (35.7)		3 (21.4)		.4
Vitreoretinal traction	8 (57.1)		3 (21.4)		.05[b]

Values are mean ± standard deviation or n *(%) unless specified.*
[a]*According to the Standardization of Uveitis Nomenclature Working Group criteria.* [b]*Statistically significant results.*

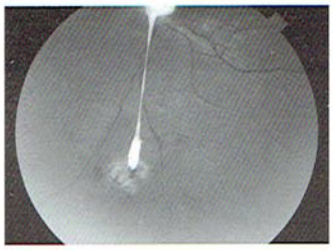

Figure 1. Posterior granuloma secondary to ocular toxocariasis. *(Image courtesy of Dr. Daniel Berinstein.)*

suggesting that a better prognosis is more likely to follow an early diagnosis of OT. None of the participants reported direct contact with pets; thus, an OT diagnosis should not be dismissed merely because a patient lacks close contact with pets.

While ME may be the most common complication of adult OT, other atypical features can also delay diagnosis. Serology in association with WB analysis of ocular samples can be beneficial in uncertain cases.

Despreaux R, Fardeau C, Touhami S, et al. Ocular toxocariasis: clinical features and long-term visual outcomes in adult patients. Am J Ophthalmol *2016;166:162-168.*

Visual Outcomes in Cancer Treatment with MEK Inhibitors

The use of mitogen-activated protein kinase (MEK) inhibitors to treat systemic cancer is associated with prolonged survival rates, but patients have experienced several adverse effects in response to MEK inhibitors, including the presence and accumulation of subretinal fluid (SRF). Weber et al from Walter Reed National Military Medical Center, Maryland, aimed to determine whether the presence of SRF associated with MEK inhibitor use correlated with visual acuity and symptoms.

The 51 participants (average age, 60 ± 13 years; 65% women) who underwent clinical trials from February 2012 to January 2014 had locally advanced or metastatic cancer, and underwent treatment in 1 of 4 clinical trials that investigated a twice-daily dose of 30 to 45 mg of the MEK inhibitor binimetinib with 1 of the following investigational agents: encorafenib, buparlisib, alpelisib and dactolisib. Comprehensive examinations occurred at baseline, biweekly for 2 months and then monthly until the end of the trial period.

To determine visual acuity and associated visual symptoms, the authors reviewed all medical records and associated ophthalmic imaging. Reported side effects of MEK inhibitors have included blurred vision, halos around lights and colorful visual spots. This study looked further into the suggestion that SRF development is typically asymptomatic and responds to drug-regimen reduction.

During the study,

- 90% of participants developed SRF (9 symptomatic patients, of whom 8 noted transient symptoms)
- 78% presented with SRF at the first visit after beginning binimetinib treatment
- only 4% had SRF at the last visit following cessation of binimetinib therapy (median, 60 days)

Optic coherence tomography imaging revealed SRF appearing as elevated, yellow-orange pockets beneath the interdigitation zone.

This study suggested that SRF in association with MEK inhibitors does not require interruption of this potentially life-prolonging cancer treatment. In fact, SRF may resolve without intervention. Further investigation is needed to determine the long-term effects of MEK inhibitors.

Weber ML, Liang MC, Flaherty KT, Heier JS. Subretinal fluid associated with MEK inhibitor use in the treatment of systemic cancer. JAMA Ophthalmol *2016;134:855-862.*

Risk After Cataract Surgery In Patients with Prior Anti-VEGF Injections

Intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents have transformed the treatment of retinal disease. Primary adverse effects related to anti-VEGF injection include systemic (e.g., thromboembolic events) and intraocular (e.g., endophthalmitis,

Table 2. Cox proportional hazard model results for specific outcomes after cataract surgery

	Outcome			
	RLF removal HR (95% CI)	POAG HR (95% CI)	Endophthalmitis <40 days HR (95% CI)	Endophthalmitis ≥40 days HR (95% CI)
Intravitreal injection of anti-VEGF agent	2.26 (1.19–4.30)[a]	1.48 (0.88–2.48)	2.29 (1.00–5.22)[a]	3.65 (1.65–8.05)[b]
Diabetes mellitus		1.09 (0.90–1.33)		
Diabetic retinopathy	1.25 (0.78–2.01)			
Glaucoma	1.12 (0.86–1.44)			
Pseudoexfoliation	1.77 (0.93–3.35)			
Charlson index	1.00 (0.96–1.03)	1.00 (0.98–1.03)	1.06 (1.02–1.10)[b]	1.02 (0.96–1.08)
Male	1.38 (1.08–1.77)[a]	1.37 (1.15–1.65)[b]	0.98 (0.72–1.35)	0.83 (0.52–1.33)
Black	1.07 (0.64–1.78)	3.18 (2.44–4.15)[b]	1.63 (0.97–2.75)	1.66 (0.82–3.34)
Other race	1.28 (0.77–2.12)	2.02 (1.47–2.78)[b]	1.60 (0.89–2.89)	0.46 (0.11–1.89)
Age	1.03 (1.01–1.06)[b]	1.02 (1.00–1.03)[a]	1.01 (0.98–1.03)	1.01 (0.97–1.05)

CI, confidence interval; HR, hazard ratio. Analysis also included covariates for the year of cataract surgery; none of the associated HRs were significant at conventional levels.
[a]p ≤ .05; [b]p ≤ .01.

inflammation, retinal detachment and increased intraocular pressure [IOP]) complications. Repeated intravitreal injections may cause lenticular trauma and sustained IOP elevations, which may secondarily increase primary open-angle glaucoma (POAG) rates.

Hahn et al from Duke University Medical Center, North Carolina, used data from Medicare claims to assess 3 adverse outcomes in 203,643 elderly patients who had cataract surgery from January 2009 to December 2013. The authors determined the incidence of POAG, endophthalmitis and retained lens fragments (RLFs) requiring removal following cataract surgery.

During the follow-up period, individuals with a history of anti-VEGF injections were at greater risk for complications (Table 2). Removal of RLFs occurred within 28 days of cataract surgery in 0.20% of patients. Acute endophthalmitis was diagnosed in 0.08% of patients within 39 days; within 1 year, 0.35% of patients were diagnosed with POAG and 0.18% with delayed-onset endophthalmitis.

Because intravitreal injections may be associated with a higher risk of intraoperative complications and postoperative endophthalmitis, the authors urged that practitioners performing intravitreal injections have an intimate understanding of anatomic intraocular relationships. Cataract surgeons should be aware that a history of injections may be a significant risk factor contributing to intraoperative complications. To better understand the interactions between the increased risk of postoperative endophthalmitis and the risk of general intraoperative complications, further studies are required.

Hahn P, Yashkin AP, Sloan FA. Effect of prior anti–VEGF injections on the risk of retained lens fragments and endophthalmitis after cataract surgery in the elderly. Ophthalmology *2016;123:309-315.*

SUMMER 2017

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