Lipid dominant toxic tumor syndrome

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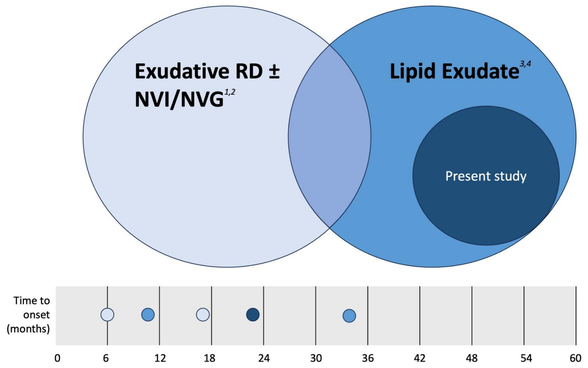
Background

- The term 'toxic tumor syndrome' (TTS) is applied to the triad of exudative retinal detachment, retinal neovascularization, and rubeosis as an acute phase response with mean time to onset of 17 months following various forms radiation following radiation therapy of choroidal melanoma.
- The treatment modalities have emphasized excision of the offending toxic tumor by transpupillary thermotherapy, endoresection, exoresection or even enucleation for advanced cases. The use of steroids and anti-VEGF agents although effective, has not been substantiated by any outcome data.
- We describe a series of patients with radiation responsive choroidal melanoma that developed lipid dominant toxic tumor syndrome. We describe the clinical features of this entity framing it as a chronic variant of toxic tumor syndrome. We also report on ocular outcomes following use of intravitreal steroids.



Methods

- A single-center, retrospective case series of patients identified to have lipid dominant exudative retinopathy following treatment of choroidal melanoma with episcleral plaque brachytherapy(EPB) from 2017 to 2024 at the Department of Ophthalmic Oncology, Cole Eye Institute, Cleveland Clinic.
- Thirteen patients where lipid exudates centered around the tumor base were identified.
- They were initially treated with intravitreal steroid injections, either Kenalog (triamcinolone acetonide 4 mg per 0.1mL, Bristol-Myers Squibb, Princeton, NJ) or Triesence (triamcinolone acetonide 4 mg per 0.1mL, Alcon Laboratories, Fort Worth, TX) and if there was partial resolution of lipid exudate, SRF, CME or improvement in measures of VA, they were transitioned to longer-acting steroid implants, Ozurdex (dexamethasone intravitreal implant 0.7 mg, Allergan, Inc, Irvine, CA) or Yutiq (fluocinolone acetonide intravitreal implant 0.18mg, EyePoint Pharmaceuticals Inc, Watertown, MA). If fully resolved by 3 months, no further steroid was injected.
- An extensive chart review was performed to collect patient demographic data tumor characteristics, radiation dose, visual acuity, OCT macular CST, number and type of treatments.
- Fundus findings were collated from ophthalmoscopic observations and fundus photographs.
- All OCT measurements were automated using the same platform (Zeiss Cirrus-HD 5000; Carl Zeiss Meditec, Dublin, CA).

Results

Table 1: Demographics, baseline characteristics, and clinical features.

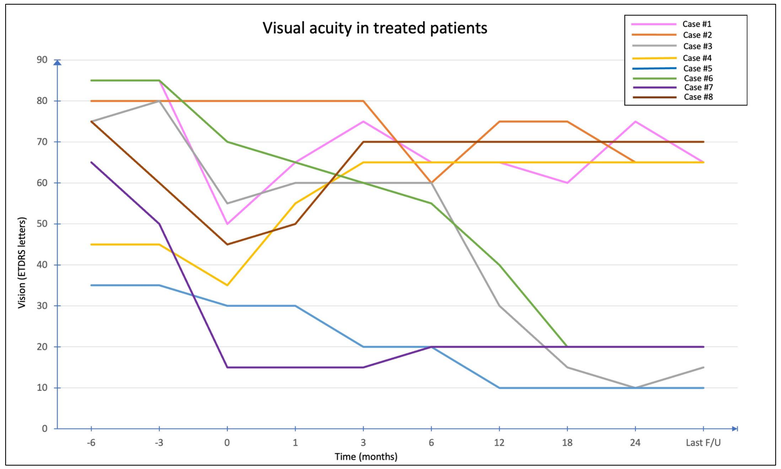
Age at diagnosis mean (range) years	54.3 (30-74)		
Gender	Male, Female		6 (46%), 7 (54%)
Laterality	OD, OS		8 (61%), 5 (39%)
Location (%)	Choroid, 13 (100%)		
Size (COMS)	Small		2 (15%)
	Medium		11 (85%)
	Large		0
Apical dose, duration	85 Gy, 72 hours		
Time to onset mean (range) months	22.1 (3-48)		
BCVA at baseline, mean (range)	67.3 (20-85)		
BCVA at diagnosis mean (range)	50.4 (10-85)		
Systemic associations	Diabetes	0	
	Dyslipidemia	High Cholesterol	6 (46%)
		High LDL	3 (23%)
		Low HDL	3 (23%)
	Hypertension	3 (23%)	
Diagnostic Features	Decrease in visual acuity		9 (69%)
	Lipid exudate		13 (100%)
	Subretinal fluid (subfoveal)		4 (31%)
	Cystoid macular edema		2 (15%)
	Exudative retinal detachment		0

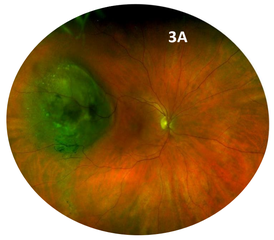
Table 2: Treatment, response, complications, and sequelae.

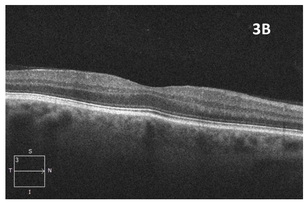
Treatment#	Observation	5 (39%)	
	Intravitreal steroids	Triesence only	3 (23%)
		Triesence → Ozurdex	2 (15%)
		Triesence → Yutiq	1 (8%)
		Triesence → Ozurdex → Yutiq	2 (15%)
Follow up duration mean (range), months	22 (3-75)		
Response to treatment	Improved/ stable vision (%)	7 (88%)	
	Reduced lipid exudate (%)	8 (100%)	
	Reduced SRF (%)	4 (100%)	
	Reduced CME (%)	1 (50%)	
Time to response mean (range), months	1.9 (1-3)		
Complications	Cataract	Requiring surgery	4 (40%)
		On observation	6 (60%)
	Ocular Hypertension	Medical management	3 (100%)
		Requiring surgery	0
	Relapse	0	
Sequelae	Proliferative Radiation Retinopathy/ NVI/NVG	3 (23%)	
	Radiation Optic Neuropathy	2 (15%)	
	Tumor recurrence	0 (0%)	
	Metastasis	2 (15%)	

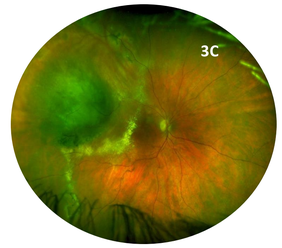
Results

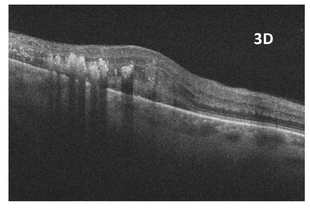
Figure 2. Visual acuity following treatment. Time 0 denotes onset of toxic tumor syndrome.

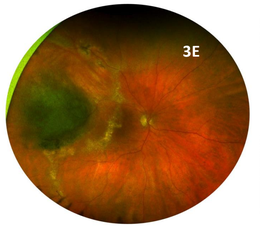












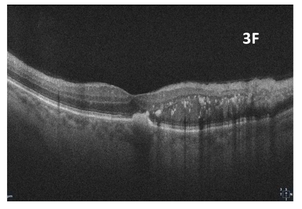


Figure 3: Fundus photographs of 62-year-old male who developed toxic tumor syndrome 27 months after treatment with episcleral plaque brachytherapy for choroidal melanoma in right eye (**A**, 11.5x10.5x4.6 mm) with normal macula (**B**). Onset of toxic tumor syndrome was heralded by marked lipid exudates (**C**) that extended into fovea (**D**). 1 month after treatment with intravitreal steroid, note reduction in lipid exudate (**E**) and partial restoration of foveal architecture (**F**).

Conclusions and Discussion

- The lipid dominant toxic tumor syndrome centered around the tumor base that occurs in a radiation responsive tumor could be considered a chronic variant in the spectrum of the toxic tumor syndrome.
- Intravitreal steroids in selected cases reverses the course of this variant, stabilizing or improving the vision, lipid exudates, subfoveal subretinal fluid and macular edema.
- Our observations would need to be verified through a larger prospective study.

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