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Clinical Features and Therapeutic Alternatives in Eyes with Secondary Vasoproliferative Tumors: A Single-Center Turkish Perspective

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SUMMARY

Aims: To evaluate retrospectively the clinical characteristics and therapeutic outcomes in eyes with secondary vasoproliferative retinal tumors (VPRT) at a tertiary center in Turkey.
Material and Methods: Patients diagnosed with secondary VPRT between 2005 and 2025 with a follow-up of 6 months or more were included. 24 eyes of 21 patients were evaluated. Their charts and multimodal imaging features were analyzed, and treatments noted.
Results: Mean age was 26.1 years (6–57). Mean follow-up was 61.1 months (6–151). Baseline BCVA was 0.77 LogMAR (0.00–2.30). VPRT was linked to non-infectious uveitis in 12 patients, retinitis pigmentosa in 5 patients, X-linked Juvenile Retinoschisis, Coats' disease, retinal dystrophy and retinopathy of prematurity in 1 patient each. The inferotemporal quadrant was the most common site (66.7%). Treatments included dexamethasone implant, transscleral cryotherapy, systemic immunosuppressive therapy, laser photocoagulation, CyberKnife, intravitreal anti-VEGF, vitreoretinal surgery, photodynamic therapy, intravitreal triamcinolone acetonide and enucleation. At baseline, 15 eyes had macular intraretinal fluid. At the final visit, dry macula was achieved in 9 of 15 eyes. Mean final BCVA was 1.01 LogMAR (0.00–3.00). Two eyes deteriorated to no light perception. One was enucleated.
Conclusion: This largest cohort of patients from Turkey with secondary VPRT reflects the diverse underlying etiologic associations and heterogeneous clinical manifestations at a tertiary center. Various therapeutic techniques were required to cope with this difficult-to-treat, challenging disease entity.
Key words: cryotherapy, CyberKnife, dexamethasone implant, intravitreal injection, laser photocoagulation, retina, vasoproliferative retinal tumor, vitrectomy

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INTRODUCTION

Vasoproliferative retinal tumors (VPRT) were first described in 1983 as presumed acquired retinal angioma in a 12-patient case series by Shields et al.[1]. Subsequently, in 1995, Shields et al. published a larger cohort of 103 patients and reported that these lesions differed clinically from classic retinal hemangiomas, as they were typically solitary, predominantly unilateral, located mostly in the peripheral inferior retina and lacking prominent feeder vessels [2]. VPRTs present as yellow-to-pink-colored solitary lesions, located in the peripheral retina and are often associated with vitritis, retinal hard exudates and hemorrhages, depending on the underlying etiology. They are classified into two groups – primary (idiopathic) or secondary [2,3]. Intermediate uveitis, retinitis pigmentosa, and Coats' disease are the most common underlying diseases in cases of the secondary type, followed by conditions such as rhegmatogenous retinal detachment, idiopathic vasculitis, familial exudative vitreoretinopathy, and other rarer entities [3–6]. Several treatment modalities were employed, depending on the nature of the disease and according to the preference of the treating ophthalmologist. In this study, we present our case series of 21 patients (24 eyes) with VPRT, focusing on the clinical features and therapeutic approaches.

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Table 1. Demographic and clinical characteristics, treatment modalities, and follow-up data of eyes with secondary vasoproliferative retinal tumors (VPRTs)

Eye	Age	Sex	Laterality	Etiology	Visual Acuity (Snellen)		Treatment Modalities									Follow-up duration (months)
					Initial	Final	Dexamethasone Implant	Anti VEGF	IVTA	Cryotherapy	Laser Photocoagulation	Immunosuppressive Treatment	CyberKnife	Vitrectomy	PDT	
1	51	M	R	Intermediate Uveitis	0.1	0.4	8	-	-	1	1	-	-	-	-	53
2	57	F	R	Posterior Uveitis	CF	0.1	3	-	-	1	-	-	-	-	-	46
3	37	F	L	Intermediate Uveitis	0.1	0.2	1	10	-	2	-	AZA	-	-	-	33
4	50	F	L	Panuveitis	0.6	1	-	-	-	-	1	AZA	-	-	-	31
5	11	F	R	Intermediate Uveitis	0.4	0.15	5	-	-	1	-	ADA	1	-	-	71
6	11	F	L	Intermediate Uveitis	0.4	NLP	1	-	-	1	-	ADA	1	-	-	53
7	17	F	R	Intermediate Uveitis	0.3	0.6	-	-	-	1	-	ADA	-	-	-	7
8	10	F	L	Retinitis Pigmentosa	0.4	0.4	-	-	-	-	1	-	-	-	-	143
9	12	F	R	Retinitis Pigmentosa	0.7	0.7	-	-	-	-	1	-	-	-	-	72
10	38	M	R	Retinitis Pigmentosa	CF	NLP	-	-	-	-	-	-	-	-	-	15
11	38	M	L	Retinitis Pigmentosa	CF	CF	-	-	1	-	-	-	-	-	-	15
12	10	M	L	XLRS	0.2	0.2	3	-	-	-	-	-	-	-	-	151
13	47	M	L	Retinitis Pigmentosa	0.2	0.25	-	-	-	-	-	-	-	-	1	114
14	16	F	R	Posterior Uveitis	0.9	0.16	2	-	-	1	-	AZA	1	2	-	144
15	16	F	L	Posterior Uveitis	0.9	0.5	1	-	-	1	-	AZA	1	2	-	144
16	8	F	L	Retinal Dystrophy	1.0	1.0	-	-	-	-	1	-	-	-	-	55
17	40	M	L	Retinitis Pigmentosa	HM	HM	1	-	-	1	-	-	-	-	-	50
18	11	M	R	Coats' Disease	0.1	CF	4	5	-	1	3	-	1	1	-	37
19	6	M	R	Retinopathy of Prematurity	0.4	0.4	-	3	-	4	1	-	-	-	-	49
20	28	M	L	Intermediate Uveitis	0.2	CF	1	-	-	1	-	-	-	-	-	6
21	36	F	L	Intermediate Uveitis	CF	CF	2	-	-	-	2	ADA	-	-	-	7
22	23	M	R	Intermediate Uveitis	0.15	HM	4	-	-	2	-	-	1	-	-	39
23	18	F	R	Intermediate Uveitis	1.0	0.9	-	1	-	-	4	MTX	-	-	-	80
24	22	M	R	Intermediate Uveitis	0.2	0.2	3	-	-	-	-	ADA	-	-	-	51

Numbers under treatment modalities indicate number of treatment sessions.
R – right, L – left, M – male, F – female, CF – counting fingers, HM – hand motion, NLP – no light perception, IVTA – intravitreal triamcinolone acetonide, ADA – adalimumab, AZA – azathioprine, MTX – methotrexate, PDT – photodynamic therapy, VPRT – vasoproliferative retinal tumor, XLRS – X-Linked Juvenile Retinoschisis, Anti-VEGF – anti-vascular endothelial growth factor

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MATERIAL AND METHODS

This study is a retrospective case series of patients who received a diagnosis of secondary VPRT between January 2005 and September 2025 at a single tertiary university hospital in Turkey. We adhered to the ethical standards of the Declaration of Helsinki. Institutional Review Board approval was obtained (Date:10.27.2025, Number: 2025/37-02). The medical records of all patients who received a clinical diagnosis of secondary VPRT were meticulously reviewed. Although a total of 27 eyes were identified, 3 eyes were excluded due to the short follow-up duration. Thus, 24 eyes of 21 patients with a follow-up of at least 6 months comprised the study group. Demographic data, clinical features, imaging characteristics and treatment techniques were recorded in detail. VPRT was considered as secondary, when associated with an identifiable predisposing ocular condition. Visual acuity was measured, using the Snellen chart and then converted to logMAR units. Applanation tonometry and dilated fundus examination were performed. Color fundus photography (Visucam 500; Carl Zeiss Meditec, Jena, Germany) and spectral domain optical coherence tomography (SD-OCT) (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) were performed at almost every examination, and fluorescein angiography (FA) (HRA 2; Heidelberg Engineering, Heidelberg, Germany) was performed at the initial visit and whenever necessary. Demographic characteristics were summarized on a per-patient basis (n = 21), whereas clinical outcomes (BCVA, tumor regression, complications) and follow-up duration were summarized on a per-eye basis (n = 24).

RESULTS

Eleven patients were female (52.4%) and ten were male (47.6%). Mean age was 26.1 years (range 6–57 years) at presentation. Table 1 summarizes the demographic data and clinical characteristics of the study group. The underlying diseases are shown in Table 2. The most common etiology was intermediate uveitis (9 patients, 42.9%), followed by retinitis pigmentosa (5 patients, 23.8%). The mean follow-up duration was 61.1 months (range 6–151 months). At the time of diagnosis, the mean BCVA was 0.77 LogMAR (range 0.00–2.30). The mean final BCVA was 1.01 LogMAR (range 0.00–3.00). Mean intraocular pressure at presentation was 15.3 mmHg (range 10–35 mmHg). Persistent elevation of intraocular pressure was not observed in any of the eyes during the follow-up, except for a single eye that developed refractory glaucoma with severe exudative retinal detachment and eventually underwent enucleation. Each eye had only a single tumor, whereas bilateral eye involvement was observed in three cases. The most prevalent site of VPRT localization was the inferotemporal quadrant (16 eyes, 66.7%), followed by superotemporal (6 eyes, 25%), superonasal (1 eye, 4.2%), and inferonasal (1 eye, 4.2%) quadrants. At baseline, there was macular intraretinal fluid in 15 of 24 eyes (62.5%) on OCT. At the last visit, dry macula could be achieved in 9 of these 15 eyes (60.0%), whereas 6 eyes (40%) showed signs of some residual fluid. Eight of nine eyes without any intraretinal fluid at presentation maintained their dry status, whereas only a single eye developed new-onset fluid formation.

Distribution of the treatment techniques is summarized in Table 3. The most frequently used treatment modality was intravitreal dexamethasone implant, administered

Table 2. Distribution of etiologies associated with secondary VPRTs in our cohort (n = 21)

Etiology	Patients (n = 21)	Patients (%)
Intermediate uveitis	9	42.9 %
Retinitis pigmentosa	5	23.8 %
Posterior uveitis	2	9.5 %
X-linked juvenile retinoschisis (XLRS)	1	4.8 %
Panuveitis	1	4.8 %
Retinal dystrophy (other)	1	4.8 %
Coats disease	1	4.8 %
Retinopathy of prematurity (ROP) sequelae	1	4.8 %

VPRT – vasoproliferative retinal tumor

Table 3. Treatment modalities applied in eyes with secondary VPRTs, including frequency of use and mean number of applications per treated eye

Treatment	Eyes treated, n (%)	Administration or sessions per treated eye, mean (range)
Dexamethasone implant	(58.3%) 14 eyes	2.79 (1–8)
Cryotherapy	(54.2%) 13 eyes	1.38 (1–4)
Systemic Immunosupression	(41.6%) 10 eyes	-
Laser Photocoagulation	(37.5%) 9 eyes	1.7 (1–4)
Stereotactic Radiosurgery	(25%) 6 eyes	1 (single session)
Anti-VEGF injection	(16.7%) 4 eyes	4.75 (1–10)
Vitreoretinal Surgery	(12.5%) 3 eyes	1.67(1–2)
Photodynamic Therapy	(4.2%) 1 eye	-
Intravitreal Triamcinolone (IVTA)	(4.2%) 1 eye	-
Observation*	(4.2%) 1 eye	-
Enucleation	(4.2%) 1 eye	-

VPRT – vasoproliferative retinal tumor, IVTA – intravitreal triamcinolone acetonide

**Cryotherapy was planned but not yet performed in one eye that received IVTA; only the IVTA session was included in the data*

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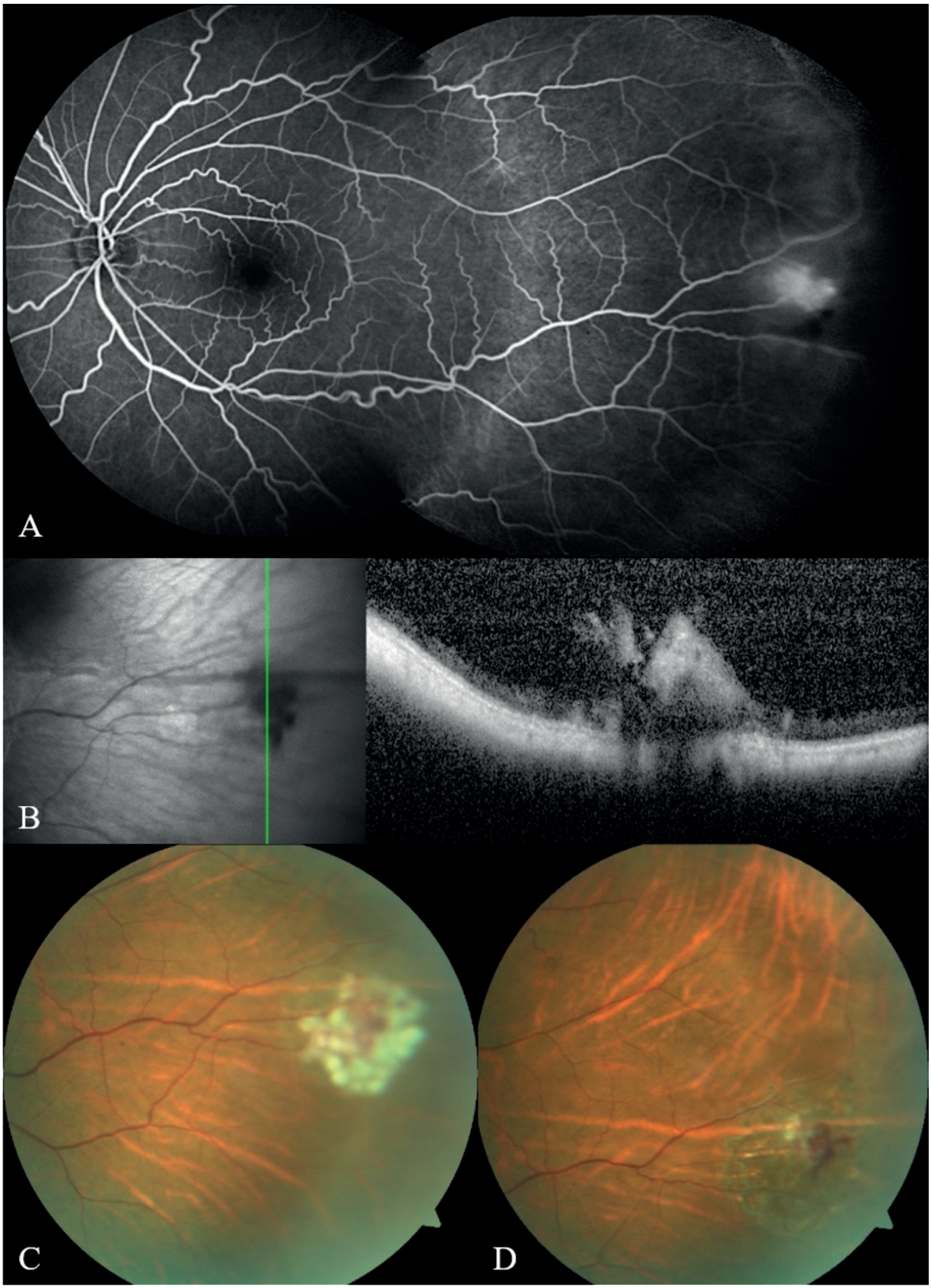


Figure 1. Eye 4, left, at presentation; (**A**) Late-phase composite fluorescein angiogram showing the hyperfluorescent VPRT related to leakage. (**B**) OCT image demonstrating the hyperreflective elevated lesion at the temporal periphery. (**C**) Color fundus photograph taken immediately after the laser photocoagulation showing the treated VPRT. (**D**) Color fundus photograph disclosing the regressed lesion with some intraretinal hemorrhage one month after the photocoagulation

VPRT – vasoproliferative retinal tumor

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at least once in 14 eyes (58.3%), with a mean of 2.79 implants among the treated eyes (range, 1–8). Transscleral cryotherapy was performed in 13 eyes (54.2%), with a mean of 1.38 sessions among the treated eyes (range 1–4). Systemic immunosuppressive therapy was administered in 10 uveitic eyes. Laser photocoagulation was performed in 9 eyes (37.5%), with a mean of 1.7 sessions (range 1–4). Stereotactic radiosurgery was used in 6 eyes (25%), each in a single session. Anti-VEGF therapy was administered in 4 eyes (16%) with a mean of 4.75 injections (range 1–10). Vitreoretinal surgery was performed in 3 eyes (12.5%), photodynamic therapy in 1 eye (4.2%), and intravitreal triamcinolone acetonide injection in 1 eye (4.2%). Enucleation was required in 1 eye (4.2%), following chronic retinal detachment and refractory secondary glaucoma in a patient who had refused cryotherapy at first. Representative multimodal imaging findings of selected cases are presented in Figures 1–6.

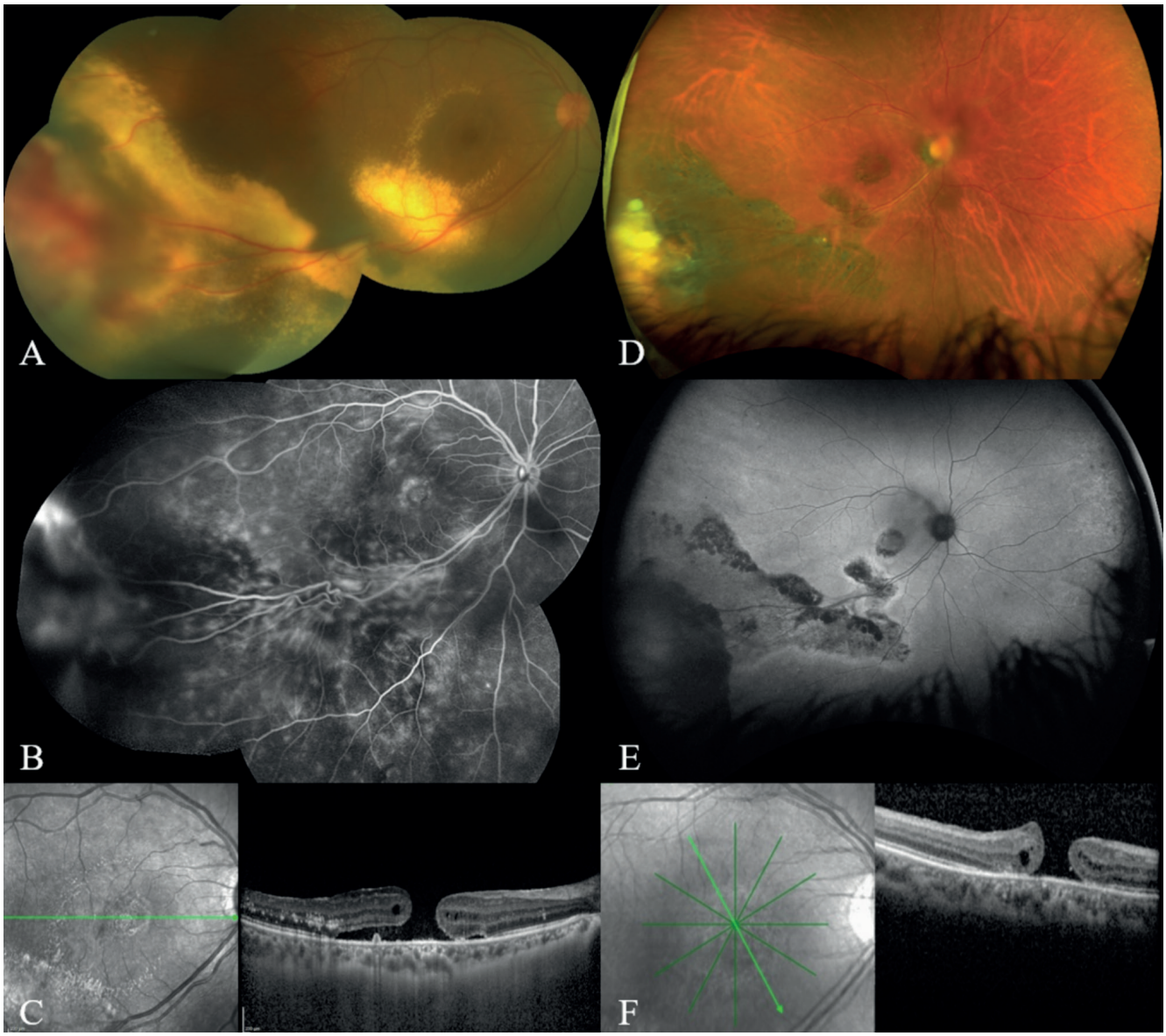


Figure 2. Eye 2, right, at presentation; (**A**) Composite color picture delineating the inferotemporally located VPRT with massive exudation. (**B**) Late phase composite fluorescein angiogram demonstrating the diffuse retinal leakage, staining of the macular hole and VPRT. (**C**) OCT image showing the large full thickness macular hole with serous retinal fluid. At the last visit; (**D**) Ultra-wide field color fundus picture delineating the quiescent looking posterior pole with scarred VPRT. (**E**) Ultra-widefield autofluorescent image showing the laser scars, hypofluorescent looking VPRT and the round macular hypofluorescent hole. (**F**) OCT section passing through the fovea disclosing the hole without surrounding serous fluid

VPRT – vasoproliferative retinal tumor

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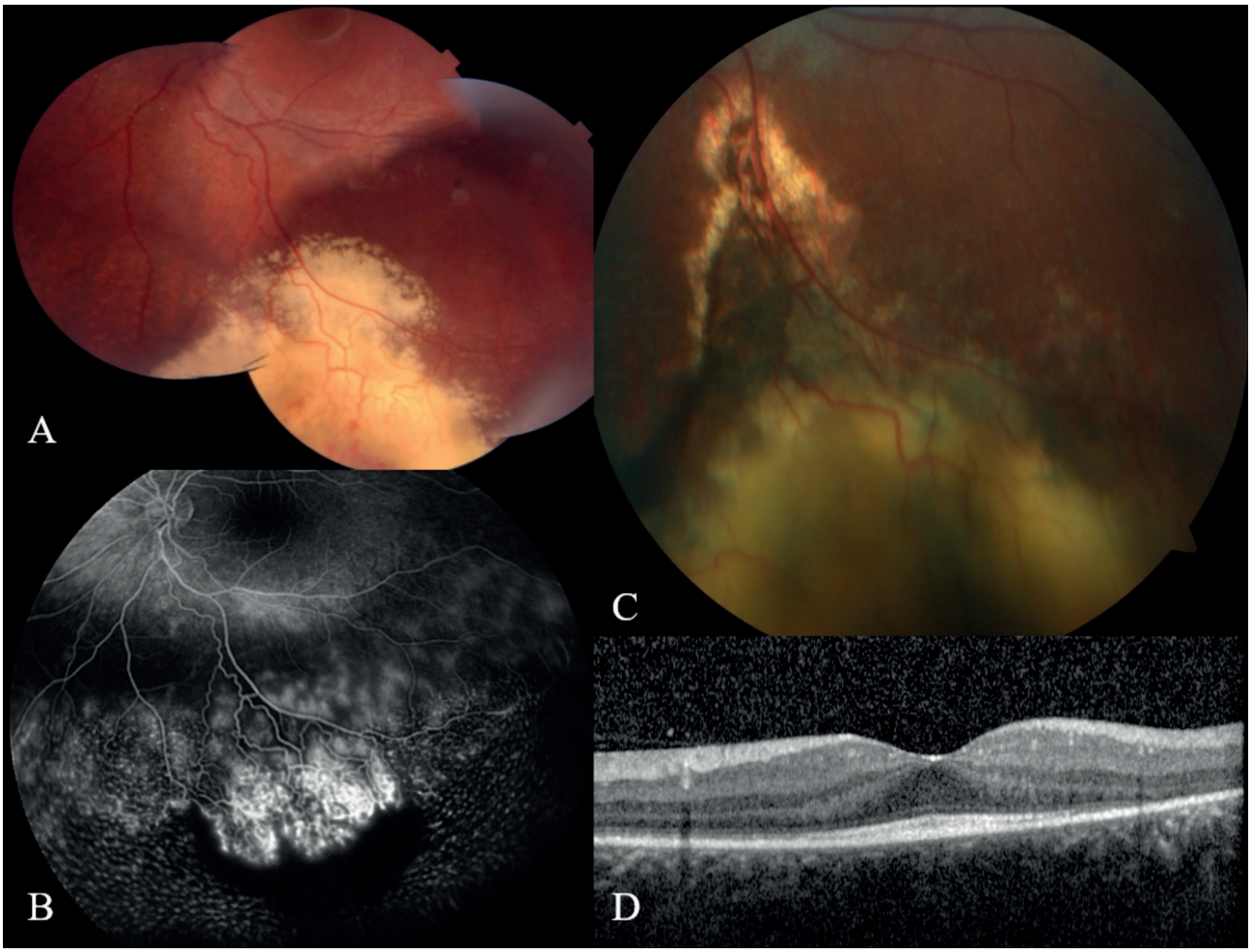


Figure 3. Eye 16, left, at presentation; (**A**) Composite color photograph showing the massive exudation, tip of the inferiorly located VPRT with intact macula. (**B**) Late-phase composite fluorescein angiogram demonstrating the diffuse inferior retinal leakage at the last visit. (**C**) Color fundus photograph demonstrating the extensive chorioretinal scarring with totally ablated VPRT. (**D**) Fovea was normal on OCT

VPRT – vasoproliferative retinal tumor

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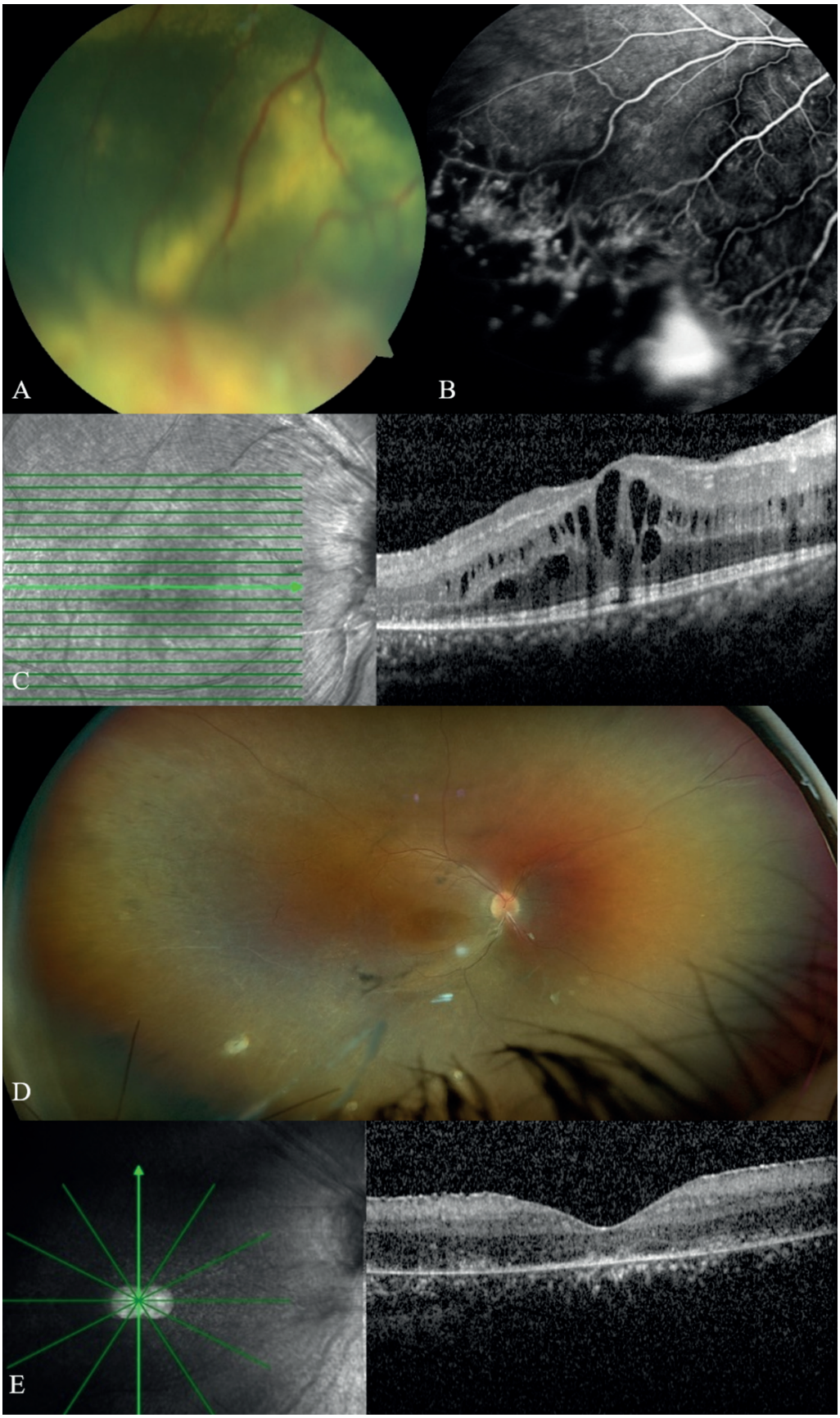


Figure 4. Eye 5, right, at the presentation; (**A**) Color fundus photograph showing the extensive exudation with an inferiorly located VPRT. (**B**) Late venous phase fluorescein angiogram demonstrating the blocked hypofluorescence related to exudation in association with the leakage. (**C**) Macular OCT section delineating the marked macular edema. (**D**) At the last visit, ultra-wide field color fundus photograph depicting the quiescent posterior pole. (**E**) OCT section through the fovea disclosing the almost normal contoured fovea

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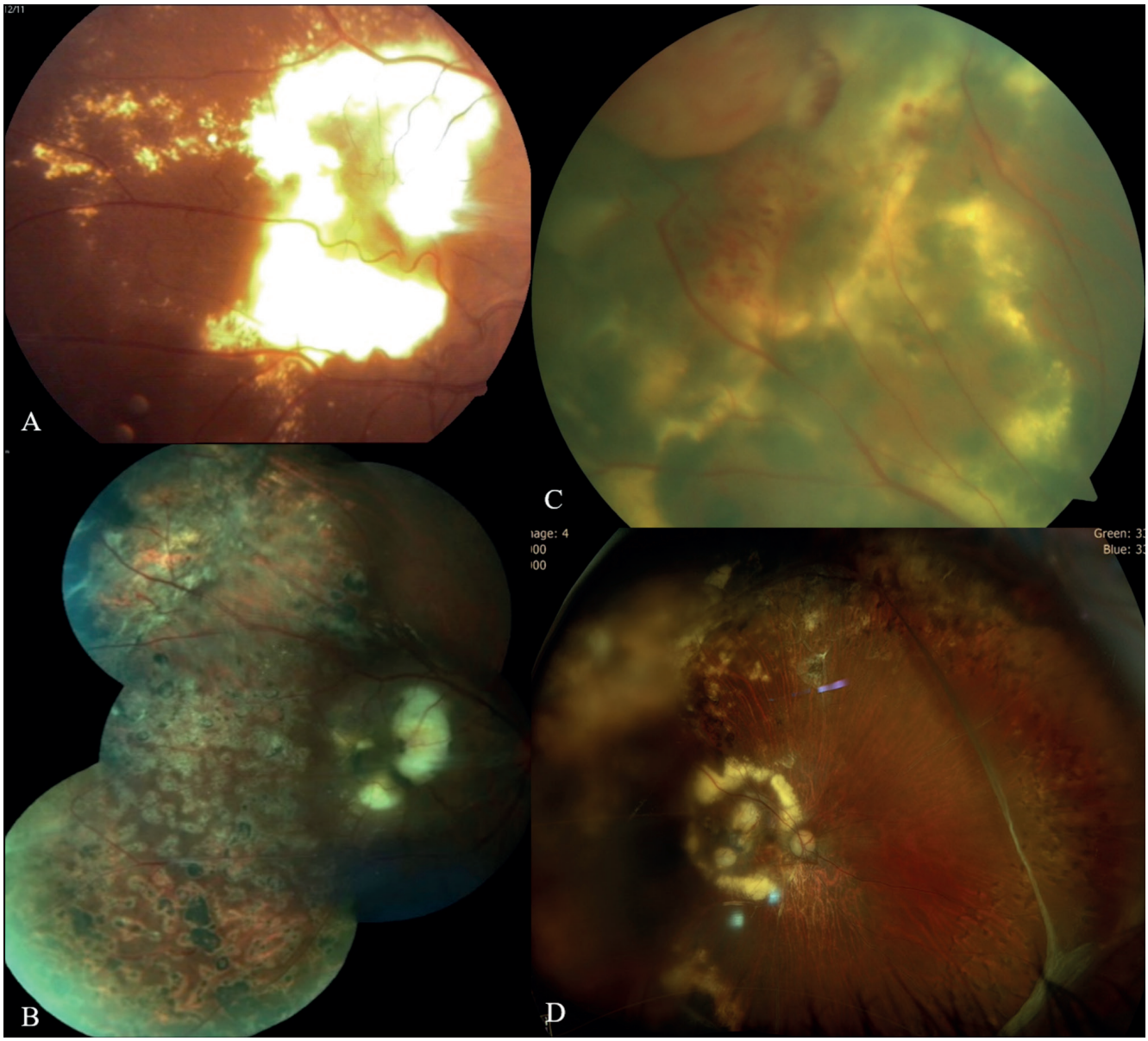


Figure 5. Eye 18, right, at presentation; (**A**) Color fundus photograph showing the massive exudation at the posterior pole with the subfoveal nodule. (**B**) Color fundus photograph two years later demonstrating the residual foveal scar with widespread retinal laser scars. (**C**) Color fundus photograph 11 years later showing recurrence related to VPRT. (**D**) Ultra-wide field color fundus photograph obtained following the vitreoretinal surgery performed 14 years after the initial presentation demonstrating the relatively quiescent right fundus

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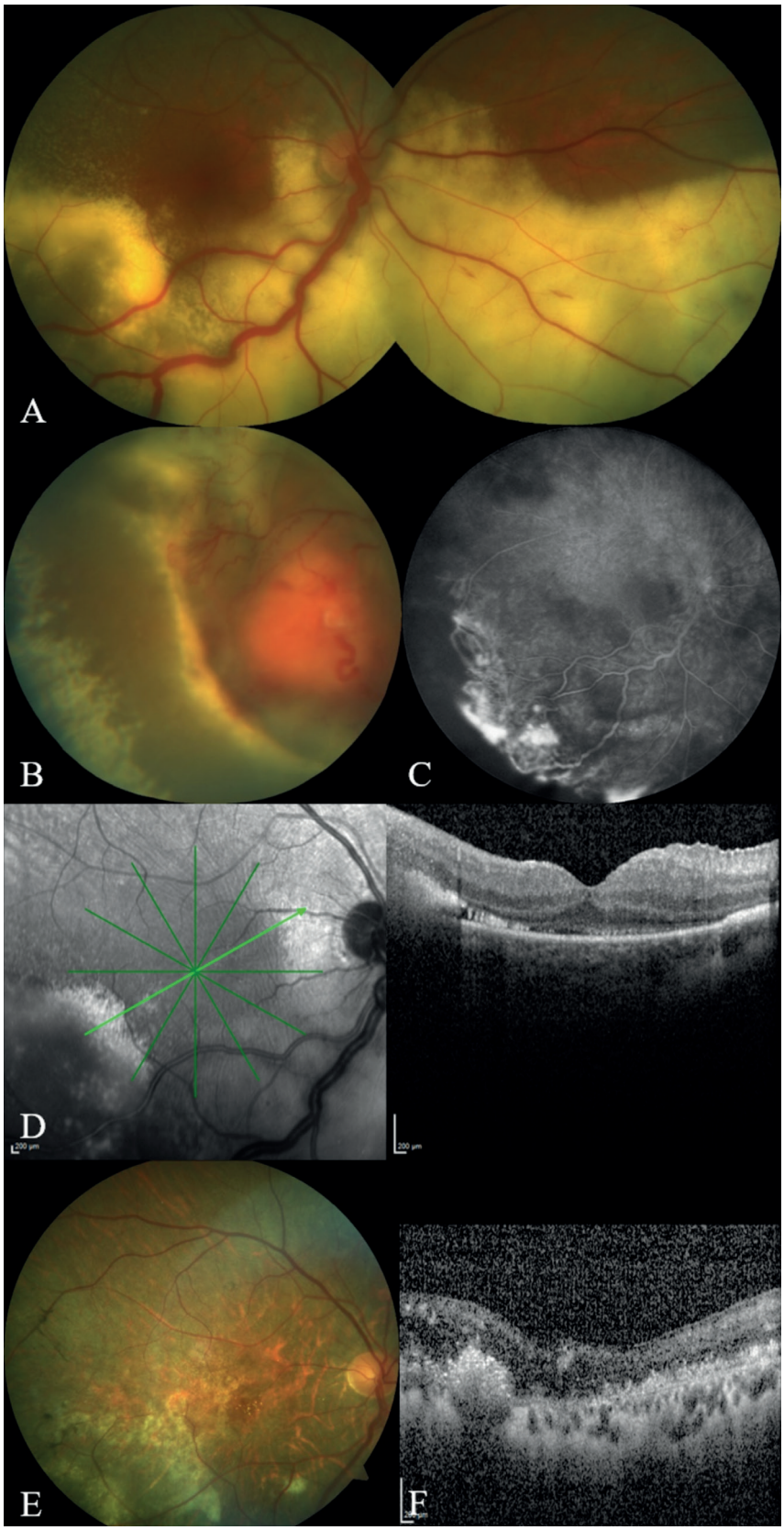


Figure 6. Eye 22, right, at presentation; (**A**) Composite color fundus photograph showing massive exudation at the inferior half of the fundus with the intact macula. (**B**) VPRT with surrounding retinal detachment at the inferotemporal fundus. (**C**) Fluorescein angiogram depicting the blocking effect of hard exudate conglomerates and hyperfluorescence related to VPRT. (**D**) Optical coherence tomographic section showing the normal contour of the macula at the last visit. (**E**) Color fundus photograph reflecting the near-total resolution of the hard exudates. (**F**) OCT illustrates diffuse inner and outer retinal atrophy and resolution of exudation

VPRT – vasoproliferative retinal tumor

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DISCUSSION

Our study demonstrates the clinical characteristics and management of secondary VPRTs in a Turkish patient cohort, representing the largest single-center perspective from Turkey. As a tertiary referral center specialized in retina and uveitis care, our cohort consisted of relatively young patients (mean age 26.1 years), and the distribution of underlying diseases reflected this demographic pattern. In our cohort, various types of uveitis were found to be the most frequent underlying cause (57.1%). Table 4 summarizes the findings of several important past studies on secondary VPRTs, along with our own data. The variations seen in these studies reflect different population characteristics and referral patterns among the reporting centers. However, uveitis and retinitis pigmentosa seem to be the most likely causes of secondary VPRTs. The presence of rare associations, such as XLRS and ROP, further illustrates the heterogeneity of secondary VPRT causes and underlines the necessity of determining the status of pre-existing diseases in affected patients.

Multimodal imaging techniques were utilized in our study group. In many cases, the type of therapeutic intervention was determined on the basis of the presence or absence of macular involvement. Macular involvement was a common finding in our cohort in 15 of 24 eyes (62.5%). At the last visit, dry macula could be achieved in 9 of these 15 eyes (60%), whereas 6 eyes (40%) showed signs of residual fluid. Eight of nine eyes without any intraretinal fluid at presentation maintained their dry status, with only a single eye developing new fluid accumulation at the follow-up.

Intravitreal dexamethasone implants and cryotherapy emerged as the two most commonly used treatment regimens, followed by systemic immunosuppressive treatment in non-infectious uveitic cases in our study group.

Table 4. Summary of major studies reporting secondary VPRTs, with our data shown in the last column

Study (Year, n = eyes)	Shields et al. (2013, 67 eyes)	Walinjkar et al. (2018, 13 eyes)	Pichi et al. (2020, 36 eyes)	Kiri et al. (2023, 25 eyes)	Ahmed et al. (2024, 18 eyes)	Submarinan et al. (2025, 16 eyes)	Our Study (24 eyes)
Etiology							
Intermediate Uveitis	14	2	36	1	9	3	10
Retinitis Pigmentosa	15	-	-	3	-	-	6
Coats' Disease	11	2	-	7	-	6	1
Rhegmatogenous Retinal Detachment	8	-	-	8	-	-	-
Idiopathic Retinal Vasculitis	4	2	-	1	4	2	-
Retinal Vasculitis Secondary to Tuberculosis	-	-	-	-	1	-	-
Familial Exudative Vitreoretinopathy	3	2	-	2	-	2	-
Posterior Uveitis	-	-	-	-	-	-	3
Toxoplasmosis	3	-	-	-	-	-	-
Aniridia	2	-	-	-	-	-	-
Congenital Hypertrophy of RPE	2	-	-	-	-	-	-
Choroiditis	2	-	-	-	2	-	-
Retinopathy of Prematurity	2	-	-	-	-	-	1
Histoplasmosis	1	-	-	-	-	-	-
Polypoidal Choroidal Vasculopathy	-	2	-	-	-	-	-
Traumatic Chorioretinopathy	-	1	-	-	-	2	-
Vascular Occlusion	-	-	-	2	-	1	-
X-linked Retinoschisis	-	-	-	-	-	-	1
Retinal Dystrophy	-	-	-	-	-	-	1
Panuveitis	-	-	-	-	1	-	1
Retinitis (Toxocara)	-	-	-	-	1	-	-
Papillitis	-	2	-	-	-	-	-

VPRT – vasoproliferative retinal tumor, RPE – retinal pigment epithelium

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However, ablative methods such as cryotherapy, laser, or photodynamic therapy were often required as the first-line therapeutic approaches to achieve durable tumor regression [7–11]. Thus, intravitreal dexamethasone was an adjunctive treatment modality and was not a definitive therapy. Accordingly, several case reports have demonstrated the beneficial effect of dexamethasone implants in addition to ablation [7,8,12].

Cryotherapy was employed in 13 eyes (54.2%), emerging as the major ablation technique preferred in our series. This is consistent with the prior large series, in which cryotherapy was reported as the most frequently employed ablative treatment for VPRTs [2,4,5,13]. Manjandavida et al. shared their experience on the effect of a single session (double freeze-thaw) cryotherapy in 16 eyes of 16 patients with VPRT (12 primary and 4 secondary types) [14]. Tumor regression was obtained in all eyes and even epiretinal membrane release was noted in 10 eyes (63%). Walinjkar et al. employed cryotherapy in 4 eyes with secondary VPRT, of which 1 developed rhegmatogenous retinal detachment, requiring vitreoretinal surgery [5]. Cryotherapy is effective in inducing tumor regression, particularly for peripheral lesions, although it may require several sessions. Our findings also confirmed the favorable effect of cryotherapy.

Laser photocoagulation was generally reserved for small or more posteriorly located tumors, often in combination with other therapies, such as dexamethasone implants or anti-VEGF injections [9]. Laser photocoagulation was performed in 9 eyes (37.5%) in our group as an ablative treatment. While laser treatment alone rarely achieved complete regression, it was useful for stabilizing lesions and reducing vascular leakage, particularly when adjunctive therapy was employed. In only one eye, a single session of laser photocoagulation was the only treatment to successfully achieve VPRT obliteration.

In our cohort, systemic immunosuppressive therapy was required in 9 out of 12 patients with uveitis-associated VPRTs (75%). Local intraocular inflammation control was achieved in the remaining 3 patients, using an intravitreal dexamethasone implant without employing systemic therapy. Pichi et al. reported the use of systemic immunosuppression in more than 90% of intermediate uveitis cases (36 eyes) complicated by VPRTs, often in conjunction with local therapies, such as cryotherapy and laser photocoagulation [15]. In contrast, Ahmed et al. treated nearly all uveitic patients with secondary VPRTs (16 of 17 eyes) with systemic corticosteroids, but only 6 eyes required additional immunosuppressive agents [16].

Stereotactic radiosurgery using the CyberKnife was performed in 6 eyes (25%) in our group. As a frameless and non-invasive method delivering focused radiation, the CyberKnife represented a novel therapeutic option in our cohort, differing from traditional radiotherapy approaches, such as iodine-125 or ruthenium-106 plaque brachytherapy that require surgical placement [17]. We administered CyberKnife treatment in eyes unresponsive to conventional methods in our group. Schmelter et al. reported good visual and anatomic outcomes following CyberKnife therapy for VPRTs in a group of 4 eyes of 4 patients [17]. They observed stabilization or an increase in visual acuity in all eyes, with tumor thickness regression and increased internal reflectivity which served as a marker of increasing fibrosis. Among the 6 eyes treated with CyberKnife, tumor regression was observed in all cases, although improvement in visual acuity was limited, with only 1 eye showing measurable gain. Despite anatomical response, one patient's vision deteriorated to no light perception at follow-up, while another required vitreoretinal surgery in both eyes for progressive tractional changes.

Vitreoretinal surgery was employed in 3 eyes (12%) in our group for eyes with advanced disease, mostly featuring severe tractional changes. Mares et al. reported the outcomes of vitreoretinal surgery in 17 eyes of 17 patients with VPRTs to achieve tumor control or to combat several complications, such as epiretinal membrane, retinal detachment, and vitreous hemorrhage [18]. However, only 9 subjects exhibited a secondary type of VPRT. The prevalence of underlying diseases was as follows: 6 cases of uveitis, 2 cases of chronic detachment, and 1 case of retinitis pigmentosa. They suggested that vitreoretinal surgical techniques might be beneficial in patients with large active VPRTs and associated complications refractory to conservative treatment or not amenable to less invasive treatment modalities.

The present study has several limitations. Firstly, it was retrospective and the study population was small. Secondly, the study spanned almost 20 years, during which time diagnostic modalities and treatment techniques showed significant changes, such as the addition of anti-VEGFs, dexamethasone implants and CyberKnife surgery. Therefore, treatment approaches were tailored on a case-by-case basis. Thirdly, quantitative tumor size measurements could not be performed in most cases. Moreover, being a tertiary referral center, we might have dealt with more severe cases, which could have adversely affected treatment outcomes. Despite these limitations, our study provides the outcomes of the largest series on secondary VPRT from Turkey, enabling us to make a comparison with other studies.

CONCLUSIONS

Ablative modalities (cryotherapy, laser, radiosurgery) remain the essential treatment methods in order to provide tumor regression in eyes with secondary VPRTs, and the ablation type can be selected according to the tumor size, location, and coexisting pathology. In uveitic patients, disease control with local and/or systemic steroids and immunosuppressive treatment can be achieved. In most eyes, combined treatment approaches should be used, including vitreoretinal surgery and radiation therapy.

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