Case Report

Hypertension: A Cause of Bilateral Proliferative Retinopathy

Eric E. Jung[1], **Hossein Ameri**[1]

[1]Department of Ophthalmology, USC Roski Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

Abstract

Purpose: To describe the case of a 67-year-old female with proliferative retinopathy secondary to uncontrolled hypertension.

Methods: Retrospective case report including multimodal imaging.

Results: A 67-year-old female presented with mild vitreous hemorrhage, retinal hemorrhage, hard exudate of the left eye and hard exudate, copper wiring of vessels, and retinal hemorrhages in the right eye. Optical coherence tomography depicted macular edema of both eyes. Fluorescein angiography revealed large areas of peripheral retinal ischemia and neovascularization with multiple areas of vascular leakage in both eyes.

Conclusions: Proliferative hypertensive retinopathy has been rarely reported in the literature. Our patient exhibited findings consistent with proliferative retinopathy secondary to hypertensive retinopathy.

Keywords: Fluorescein angiography, Hypertensive retinopathy, Macular edema, Proliferative retinopathy, Retinal neovascularization, Vitreous hemorrhage

Address for correspondence: Hossein Ameri, USC Roski Eye Institute, 1450 San Pablo St., Los Angeles, California 90033, USA.
E-mail: ameri@med.usc.edu
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Introduction

Hypertension causes vascular damage throughout the body, and hypertensive retinopathy is typically characterized by fundoscopic findings such as arteriolar narrowing, arteriovenous nicking, retinal hemorrhages, hard exudates, and macular edema.[1] Neovascularization and resulting sequelae such as vitreous hemorrhage are not classically associated with hypertensive retinopathy.

Case Report

A 67-year-old female with a past medical history of uncontrolled hypertension for 15 years and end-stage renal disease on peritoneal dialysis for 2 years presented to the emergency department with 3 days of chest pain. She also reported acute worsening of chronically blurry vision in both eyes since the previous day. She noted that she had skipped her peritoneal dialysis for a few days.

Past ocular history was notable for bilateral cataracts, but no other known diagnoses. Past surgical history was notable only for a prior cesarean section. She denied any home medications or any ethanol, tobacco, or recreational drug use. Her blood pressure was 220/150 mm of mercury (mmHg) on presentation to the emergency department, and her initial presentation was concerning for possible myocardial infarction and hypertensive emergency with troponin leak. She was admitted to the telemetry floor.

On ophthalmologic examination, her best-corrected visual acuity was 20/200 in the right eye and 20/200 in the left eye. Intraocular pressure was 14 by tonometry in both eyes. Pupils were equal, round, and reactive without any afferent pupillary defect. Extraocular movements were full bilaterally, as were gross visual fields by confrontation. Slit-lamp exam was notable for nuclear sclerotic cataracts with vacuoles in both eyes, but otherwise unremarkable. Dilated fundus examination was notable for slightly enlarged cup-to-disc ratios, attenuated

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vessels, copper-wiring of arteries, microaneurysms, blot hemorrhages, and hard exudates in both eyes. In the left eye, areas of superonasal neovascularization and inferior vitreous hemorrhage were noted. Close interval examination while inpatient was planned, but the patient was discharged from the hospital after myocardial infarction was ruled out, and she was subsequently lost to follow-up. The patient was contacted and arrived at the ophthalmology clinic 3 weeks later without change in vision.

Dilated fundus examination at this time showed clear media, mild optic nerve cupping without notching or neovascularization of the disc, a large area of nasal exudate, vessel wall opacification (copper wiring), microaneurysms, and blot hemorrhages in the right eye [Figures 1a and c]. In the left eye, significantly improved but residual trace vitreous hemorrhage was noted inferiorly, as well as mild optic nerve cupping without notching, a superonasal dot–blot hemorrhage, a small superonasal hard exudate, and a possible area of superonasal neovascularization [Figures 1b and d]. Fundus autofluorescence was obtained and demonstrated patches of hyper- and hypoautofluorescence bilaterally. The loss of a distinct foveal center was apparent, especially in the left eye [Figures 1e and f].

Optical coherence tomography of the macula was obtained and demonstrated some irregularity of the ellipsoid zone, a partial posterior vitreous detachment with focal vitreomacular traction, a nasal epiretinal membrane, scattered hard exudates, and scant extrafoveal intraretinal fluid in the right eye [Figure 2a]. The left eye exhibited slightly more intraretinal fluid with some centrally, more irregularity of ellipsoid zone, hard exudates, and a more extensive epiretinal membrane [Figure 2b].

Fluorescein angiography (FA) demonstrated large areas of capillary nonperfusion in all quadrants, and leakage in multiple areas from retinal neovascularization in both eyes, with mild disc leakage [Figure 2]. There was mild disc leakage as well. In addition, superonasal vascular remodeling suggestive of branch retinal vein occlusion was demonstrated in the left eye [Figures 2e and f]. Early phase transit FA of the left eye demonstrated early hyperfluorescence of the optic nerve, without any significant choroidal filling deficits or delayed arteriovenous transit time [Figure 3].

Overall, this patient's clinical picture was consistent with bilateral proliferative retinopathy. Her previous workup for end-stage renal disease 3 years prior resulted in the following negative laboratories: hepatitis panel, antineutrophil cytoplasmic antibody (c-ANCA/p-ANCA), antinuclear antibody, anti–glomerular basement membrane antibodies, myeloperoxidase antibodies, double-stranded DNA antibodies, proteinase-3 antibodies, rheumatoid factor, and QuantiFERON-TB Gold Plus. Complement levels and hemoglobin A1c levels were normal. The nephrology service attributed her renal disease to chronic uncontrolled essential hypertension after exclusion of vasculitic disease and autoimmune etiologies. In addition, laboratories were drawn at the most recent admission, and a complete blood count, metabolic panel, head computed tomography, and chest X-ray were normal except for mild anemia. Notable laboratories included a hemoglobin A1c of 5.9; no glucose reading above 125 mg/dL for the preceding year was observed. She had had several hypertensive episodes in the past year with several systolic blood pressure readings above 200 mmHg. Echocardiogram revealed a normal ejection fraction and was negative for valvular pathology or wall motion abnormalities.

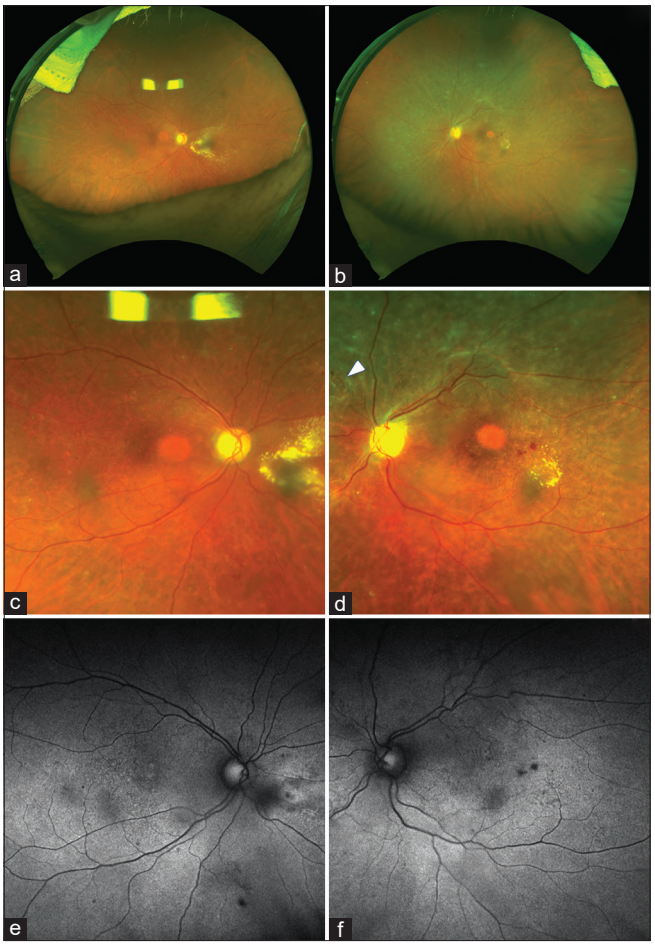

Figure 1: Optos ultra-widefield pseudo-color photos of the right eye (a) show a large area of hard exudates nasally, vessel wall opacification, microaneurysms, and blot hemorrhages. A higher magnification pseudo-color image of the right eye (c) better demonstrates the area of hard exudate. Ultra-widefield photo of the left eye (b) shows trace vitreous opacities from previous vitreous hemorrhage inferiorly, dot–blot hemorrhage, hard exudate, mild pigment irregularity superiorly, and vascular remodeling superonasally, better appreciated in the higher magnification photo (d) (white arrow). Images have been brightened postcapture to allow for better visualization of pathology, but the patient did not exhibit pale nerves on in-person examination. Optos fundus autofluorescence images demonstrate patches of hyper-and hypo-autofluorescence bilaterally (e and f)

No signs of anterior segment neovascularization were found, and given the bilaterality and presence of hard exudates, the ocular ischemic syndrome was deemed unlikely. Furthermore, early phase FA images taken during transit

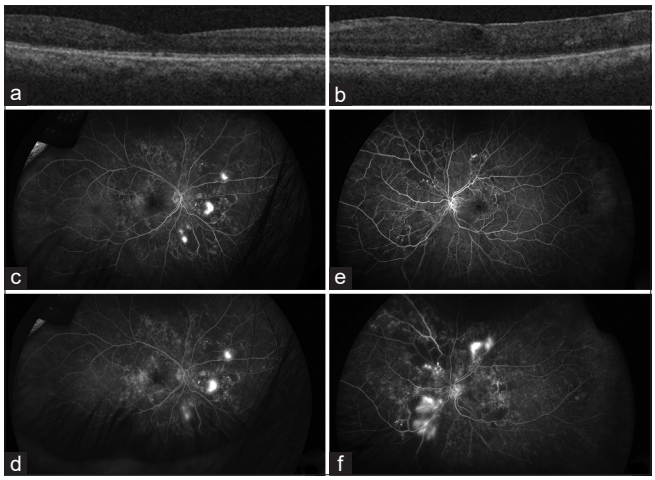

Figure 2: Spectral-domain optical coherence tomography of the macula demonstrates generalized atrophy, with some irregularity of the ellipsoid zone, a partial posterior vitreous detachment with focal vitreomacular traction, nasal epiretinal membrane, scattered hard exudates, and scant extrafoveal intraretinal fluid in the right eye (a). The left eye exhibited more intraretinal fluid, hard exudates, and a more extensive epiretinal membrane (b).(c-f) Fluorescein angiography (FA) with left eye transit demonstrates areas of capillary nonperfusion beginning in early phases and late leakage in multiple areas including mild disc leakage. A superonasal branch retinal vein occlusion was evident with nonperfusion of the entire superior quadrant (e and f). FA of the right eye demonstrates areas of capillary nonperfusion in early (b) and late (c) phases, as well as multiple areas of leakage

did not demonstrate significant choroidal filling deficits or delayed arteriovenous filling [Figure 3]. Due to a lack of other risk factors such as diabetes mellitus, vasculitic disease, or autoimmune conditions, the patient was diagnosed with proliferative hypertensive retinopathy. Given the central macular edema, intravitreal anti–vascular endothelial growth factor (anti–VEGF) therapy of the left eye was administered. In addition, panretinal photocoagulation was performed in both eyes. Follow-up 2 weeks after the administration of laser photocoagulation demonstrated a significant decrease of leakage on FA.

When seen at her follow-up visit 9 months later, the patient's eyes were clear from signs of vitreous hemorrhage, neovascularization, or macular edema. Visual acuity improved to 20/100 in the right eye and remained unchanged at 20/200 in the left eye. Her intraocular pressure was normal in both eyes, and her mild optic nerve cupping remained stable. Her persistently poor vision in both eyes was attributed to a combination of macular ischemic changes and cataracts. In addition, mild hypertensive optic neuropathy could not be ruled out as a possible contributor to her low vision. The patient had undergone right lower extremity angioplasty and subsequent lower extremity amputation 6 months after initial ophthalmologic evaluation due to the development of gangrene and peripheral arterial disease secondary to hypertension. The patient's blood pressure improved subsequently with increased compliance with medication and lifestyle modifications, and she is currently being evaluated for a kidney transplant. Explicit

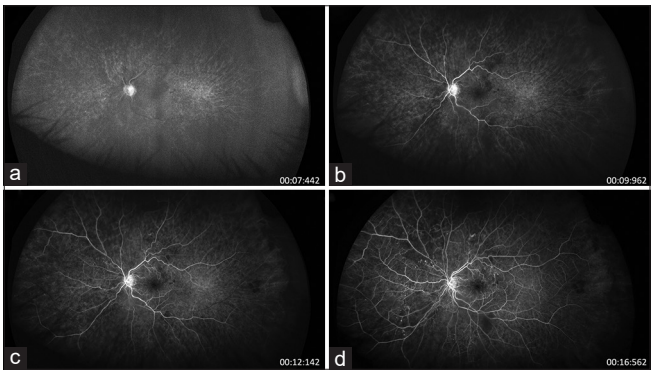

Figure 3: Fluorescein angiography of the left eye (transit eye) in early phases. The images demonstrate early hyperfluorescence of the optic nerve (a), with the filling of the choroidal and arterial vasculature (b) and arteriovenous circulation (c and d) shortly thereafter. Already, the areas of retinal nonperfusion and early leakage of vessels can be appreciated soon after the injection of fluorescein (d). Relative time is indicated by the timer in the bottom right area of each image (minutes: seconds: milliseconds) – the start time was delayed from the actual injection of intravenous fluorescein dye at the time of capture, but the relative progression demonstrates the absence of any delayed filling

consent was obtained from the patient to share her medical records and photographs for academic purposes.

Discussion

Elevated blood pressure causes a series of changes to the retinal vasculature. While not necessarily sequential, hypertension can cause vasoconstriction of retinal arterioles, sclerosis caused by intimal thickening, and hyaline degeneration leading to copper wiring and arteriovenous nicking.[1,2] Severe or longstanding hypertension can disrupt the blood–retinal barrier leading to necrosis of endothelial cells, exudation of blood and lipids, and retinal nerve fiber layer ischemia.[3]

Disruption of retinal vasculature and resulting ischemia is known to drive angiogenesis and retinal neovascularization in diseases such as diabetic retinopathy, retinal vascular occlusions, and sickle cell retinopathy. However, neovascularization is not classically described in the spectrum of hypertensive retinopathy, and only a few case reports of this so-called proliferative hypertensive retinopathy exist. Previous reports are listed in Table 1.[4-7] Our patient presented with a similar systemic blood pressure compared to previous reports. Our patient's older age, however, contrasts with the younger examples published thus far. Abu Sbeit *et al*. hypothesized that younger patients with hypertensive retinopathy might be more prone to proliferative disease due to more pliable nonhyalinized retinal vessels,[4] but our case suggests that proliferative hypertensive retinopathy is not exclusive to younger patients. There is some debate as to whether some of these reports represent prior retinal vein occlusions leading to proliferative retinopathy. This is a distinct possibility for our case as well, given the distribution of nonperfusion seen, especially in the left eye. However, a bilateral presentation as in this case would require multiple repeat insults in both eyes.

Table 1: Previous case reports of proliferative hypertensive retinopathy

Authors	Age	Sex	Type of HTN	Presenting BP*	Duration of HTN	Presentation	Ocular treatment	Outcome
Current case	67	Female	Essential, causing ESRD	220/150	17 years	20/200 OU, mild VH OD, CME OU, NVE OU	Intravitreal anti-VEGF OS, PRP OU	Clearance of VH, NV, and macular edema
Sbiet *et al*.[4]	34	Female	Essential	290/160	A few years (unspecified)	20/200 OD, 20/400 OS w/bilateral mild VH, NVE	PRP OU	20/100 OD and CF OS. Regression of NV. Stable tractional membranes
Stryjewski *et al*.[5]	Late 40's	Male	Essential	270/160	Previously undiagnosed	CF OD with dense VH, HM OS with tractional RD	None	Not available
Golshani *et al*.[6]	30	Female	Secondary to IgA nephropathy	225/115	Chronic (unspecified), requiring hemodialysis for 8 years	HM OD and CF OS, NVE	Intravitreal anti-VEGF and PRP OU	NLP OD due to NVG OD, tractional RD OS
Georgiadis *et al*.[7]	33	Male	Secondary to hyperaldosteronism	N/A	N/A	20/200 OD and 20/30 OS, NVE	Intravitreal anti-VEGF OD and PRP OS	Stabilization of vision with regression of NV

*Systolic BP (mmHg)/diastolic BP (mmHg). CF: Counting fingers vision, ESRD: End-stage renal disease, HM: Hand motion vision, HTN: Hypertension, NLP: No light perception vision, NV: Neovascularization, NVE: NV elsewhere, NVG: Neovascular glaucoma, OD: Right eye, OS: Left eye, PRP: Panretinal photocoagulation, VEGF: Vascular endothelial growth factor, BP: Blood pressure, VH: Vitreous hemorrhage, OU: Both eyes, CME: Cystoid macular edema, RD: Retinal detachment, N/A: Not available, IgA: Immunoglobulin A

In diabetic retinopathy, damage to the endothelium and pericytes of retinal capillaries occurs early on and can lead to microvascular occlusion.[8] This can cause retinal nonperfusion, and as ischemia progresses, retinal cells release VEGF to encourage the growth of new blood vessels in a process known as neovascularization. In contrast, hypertensive retinopathy is thought to be primarily a disease of arteries and arterioles in early disease.[1] Arterioles constrict as systemic blood pressure rises, as in throughout the body, leading to the sequence of changes seen in hypertensive retinopathy. However, histologic studies have demonstrated that with severely elevated blood pressure, damage and necrosis of the vessel endothelium can occur, leading to focal leakage and capillary nonperfusion.[3] This may eventually lead to enough retinal ischemia to drive neovascularization, but the severity and/or chronicity required to achieve this level may explain why this occurrence is rare in comparison to diabetic retinopathy.

Our current patient was given an intravitreal injection of bevacizumab in the left eye as well as panretinal photocoagulation laser treatment in both eyes. Similar treatment was performed in some of the prior case reports of proliferative hypertensive retinopathy [Table 1]. Over 9 months of follow-up, our patient remained clinically quiescent from further signs of proliferative retinopathy.

Our patient demonstrated profound renal disease, requiring hemodialysis. The case published by Golshani *et al*.[6] also exhibited profound renal disease, secondary to IgA nephropathy, and required hemodialysis. A link between retinopathy and nephropathy has been purported. Chillo *et al*. found that the severity of hypertensive retinopathy appears to be independently associated with chronic kidney disease severity.[9] Diabetic retinopathy severity, including the proliferative stage, also appears to be associated with the progression of chronic kidney disease in diabetes,[10] and the severity of retinopathy, in general, is independently associated with decreasing glomerular filtration rate.[11] It may be prudent to consider concurrent severe renal disease in any patient presenting with proliferative hypertensive retinopathy.

In conclusion, proliferative hypertensive retinopathy has been rarely reported in the literature. Our patient exhibited findings consistent with proliferative retinopathy secondary to hypertensive retinopathy. This presentation can resemble other more common causes of proliferative retinopathy, and a thorough workup should be performed to exclude other etiologies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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