Severe outer nuclear layer hemorrhage secondary to malignant hypertension: A case report

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ABSTRACT

Purpose: To report the first case of malignant hypertension who presented with severe outer nuclear layer hemorrhage affecting the fovea and had rapid recovery in findings after intravitreal injection of bevacizumab**.**

Case Report: A 72-year-old woman presented with complaints of blurred vision in her left eye. An extensive systemic and ophthalmic examination confirmed the diagnosis of outer nuclear layer hemorrhage caused by malignant hypertension. An intravitreal injection of bevacizumab (1.25 mg/0.05 mL) was administered to the left eye. The outer nuclear layer hemorrhage completely resolved three weeks after intravitreal bevacizumab injection treatment, and the visual acuity improved significantly.

Conclusion: Malignant hypertensive retinopathy may present with outer nuclear layer hemorrhage affecting the fovea and intravitreal anti-VEGF therapy may be beneficial in these cases.

Keywords: Malignant Hypertension, Outer Nuclear Layer Hemorrhage, Hypertensive Retinopathy.

INTRODUCTION

Malignant hypertension (MHT) is an acute form of hypertension, a serious medical condition that can cause various symptoms and complications. Hypertensive retinopathy (HR) is one of the most common consequences of MHT, which is a specific type of retinal damage caused by high blood pressure.[1] The severity of HR ranges from mild to severe, depending on the general status of the patient. Persistent hypertension causes an increase in the permeability of vessels in the retina, resulting in a range of changes in the retinal tissue such as flame-shaped hemorrhages, cotton-wool spots, hard exudates, optic disc, and macular edema.[2] Recent studies have demonstrated that HR is a reliable indicator of systemic morbidity and mortality caused by target organ damage. A study conducted by Erden et al. found that the higher the severity and longer duration of hypertension, the greater the risk of developing retinopathy.[3]

Herein, we report a patient with MHT who presented with outer nuclear layer (ONL) hemorrhage involving the fovea but recovered swiftly following intravitreal injection of bevacizumab.

Case Report

A 72-year-old woman with a history of diabetes mellitus, hypertension, and chronic kidney disease presented to our clinic with complaints of blurred vision in her left eye for five days. Due to a previous cerebrovascular stroke, she was on antiplatelet (clopidogrel) medication. She had been taking antihypertensive, and anti-diabetic medications as well. On further questioning, she reported that hemodialysis had been required for the last three years due to end-stage renal disease associated with diabetic nephropathy. She was also on heparin therapy during dialysis. Initially, her best corrected visual acuity (BCVA) was 20/25 in the right eye and 20/32 in the left eye respectively. Nuclear sclerosis was present in the right eye and a grade 1 nuclear cataract in the left eye. fundus examination In the right eye, revealed an area of retinal pigment epithelial (RPE) atrophy beneath

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the optic disc, approximately 1.5 optical disc in size, as well as arterial narrowing and focal irregularities (figure 1a); in the left eye, fundus examination revealed optic disc swelling, dense flame-shaped hemorrhage around and on the optic disc, with an approximate diameter of 3-4 optic disc, and deep retinal hemorrhage extending to the fovea (figure 1b). Optical coherence tomography (OCT) showed the presence of optic disc edema and the onset of fluid and blood accumulation in ONL and fluid accumulation in the subretinal space of the left eye and area compatible with hemorrhage in the Henle fiber layer (figure 2a). The right eye OCT examination was unremarkable. Her blood pressure was 220/130 mmHg. The patient was diagnosed with MHT and referred to the nephrology department for blood pressure regulation. As a differential diagnosis, we considered Non-arteritic Anterior Ischemic Optic Neuropathy (NAION), posterior vitreous detachment, vascular tumor, uveitis. NAION was less likely because treatment improved visual acuity considerably. The absence of posterior vitreous separation demonstrated that it was not the source of the bleeding. Because there were no inflammatory signs in the anterior chamber or vitreous cavity, uveitic entities were ruled out. Besides serological testing to rule out neuro retinitis-causing conditions such as Bartonella henselae infection, syphilis, Lyme disease, and toxoplasmosis; cranial computerized tomography and diffusion magnetic resonance imaging were also requested to exclude Terson syndrome. The results of all the requested tests were normal. On review after five days, the blood pressure could not be controlled despite appropriate treatment and she reported worsening vision in the left eye. Her BCVA was 20/25 in the right eye and 20/63 in the left eye. Fundus examination showed the progression of hemorrhage through the fovea (figure 1c). Fluorescein angiography (FA) showed window defect under the optic disc with an approximate diameter of 1.5 optic disc in the right eye (figure 3a) and hyperfluorescent areas around the fovea in the late phase in the left eye (figure 3b). FA also did not show any signs of choroidal neovascularization or macroaneurysm. The patient was treated with a single intravitreal injection of bevacizumab (1.25 mg / 0.05 ml) in the left eye. Three weeks after the treatment, BCVA in the left eye improved to 20/30. Fundus examination revealed a significant reduction in hemorrhage in the optic disc and macular area and semi-circular macular star formation (figure 1d). OCT revealed complete resolution of intra- and subretinal fluid (figure 2b).

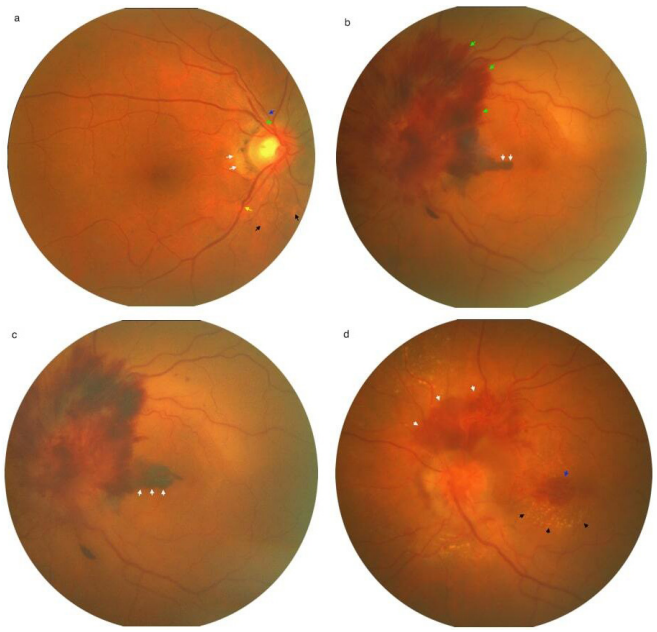

Figure 1: (a) *Fundus photograph shows thickening of walls of retinal arterioles (silver wiring) (green arrow), arteriovenous nicking area and focal narrowing (yellow and blue arrow), peripapillary atrophy area (white arrow) and retinal pigment epithelial atrophy area under the optic disc (black arrow) in the right eye on initial presentation.* **(b)** *Shows dense flame-shaped hemorrhage around the optic disc (green arrow) and deep retinal hemorrhage in the left eye on initial presentation (white arrow).* **(c)** *Shows progression of deep retinal hemorrhage from the optic disc through the fovea in the left eye on day five (white arrow).* **(d)** *Shows significant reduction in superficial hemorrhage (white arrow), regression of deep retinal hemorrhage (blue arrow), and semi-circular macular star formation in the left eye three weeks after intravitreal injection of bevacizumab (black arrow)*

DISCUSSION

Hypertension is a serious health issue that has become a global epidemic. According to the World Health Organization (WHO), the number of people with hypertension currently exceeds 1.4 billion, and is estimated to exceed 1.5 billion in 2025. Furthermore, hypertension is responsible for more than 10 million deaths per year.[4,5]

Intimal thickening and hyaline degeneration are two structural alterations that chronic hypertension causes in the arterial wall. These show up as copper or silver wiring, which are spots of opacification on the vessel wall. Nicking, or arteriovenous (AV) crossing, occurs when the venules are compressed at the point where the arterioles thicken. The retinal nerve fiber layer can develop localized patches of ischemia, resembling cotton-wool spots, due to severe hypertension.[2]

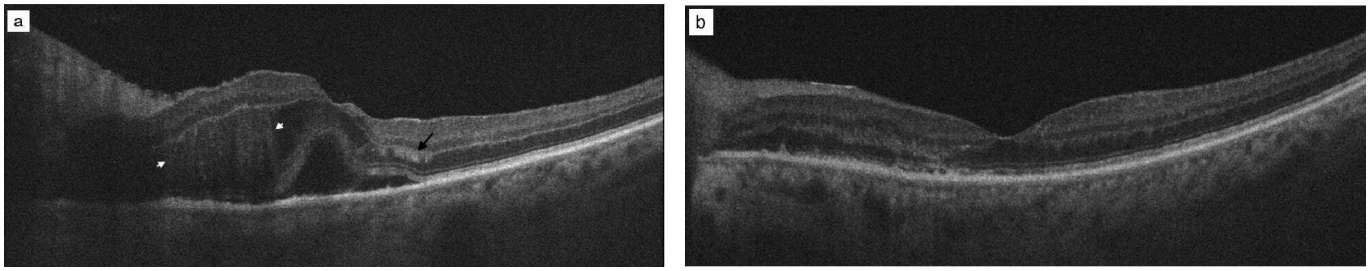

Figure 2: (a) *Optical coherence tomography reveals blood and fluid accumulation in the ONL (white arrow), a hyperreflective region in the Henle fiber layer is consistent with a hemorrhage in the Henle fiber layer (black arrow), and concomitant subretinal fluid accumulation in the left eye on day five.* **(b)** *Shows resolution of the ONL hemorrhage and subretinal fluid in the left eye three weeks after the intravitreal injection of bevacizumab.*

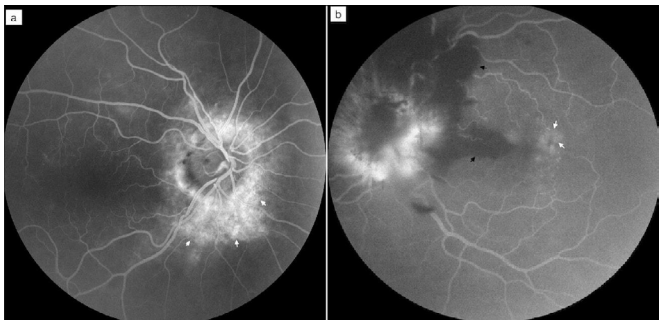

Figure 3: **(a)** *Fluorescein angiography of the right eye shows window defect under the optic disc on initial presentation (white arrow).* **(b)** *Hyperfluorescent areas around the fovea in the late phase (white arrow) and blocking effect of the hemorrhages (black arrow) in the left eye on first presentation.*

In patients with malignant hypertensive retinopathy, retinal nerve fiber layer edema, intraretinal and subretinal fluid can be observed on OCT.[6,7] The fundus findings of malignant hypertensive retinopathy patients are usually bilateral, but confusion may arise if there is unilateral, asymmetrical, or atypical finding, such as absence of the optic disc swelling, an incomplete or absent macular star, or exudative retinal detachment without bleeding or cotton wool spots.[8] Localized variations in vascular structures or individual differences in how the retinal blood vessels adapt to hypertension may contribute to this asymmetry.

The literature has reported a variety of reports indicating that malignant hypertensive retinopathy can cause retinal edema and subretinal fluid. However, we are unaware of any previous reports describing MHT accompanied by severe ONL hemorrhage. We believe that the chronic kidney disease and anticoagulant treatment disrupted the coagulation cascade balance, leading to ONL hemorrhage and dense flame-shaped hemorrhage. Chronic kidney disease patients have an elevated bleeding rate while also being susceptible to thrombosis, resulting in a paradoxical hemostatic potential.The most likely reason of increased bleeding is platelet dysfunction, which is accompanied by further involvement of the coagulation cascade due to aberrant von Willebrand factor and platelet interactions.[9]

While hypertensive retinopathy often regresses with effective blood pressure control, the rate and extent of regression vary among individuals, influenced by factors like the severity and duration of hypertension. Notably, advanced stages with significant damage, such as optic disc swelling, subretinal fluid, and concomitant hemorrhage, may potentially lead to permanent damage.

The primary approach to treat malignant hypertension is the regulation of blood pressure. However, in our case, blood pressure could not be brought back to normal limits despite treatment. The patient was administered intravitreal bevacizumab in order to minimize the toxic and destructive effects of hemorrhage on the photoreceptors. B.J. Winn et al., demonstrated that subretinal hemorrhage causes specific photoreceptor damage within 48 hours after the onset of the injury.[10]

Even though there is no definitive consensus for anti-VEGF therapy in the treatment of malignant hypertensive retinopathy (MHR), our case showed a very good response to intravitreal injection of bevacizumab, and it was predicted that this treatment might be useful, especially in cases that are resistant to treatment. Eui Yon Kim et al., reported that in two selected cases, intravitreal bevacizumab injections might be a useful adjunctive treatment for MHR.[6] Another study also showed the use of intravitreal bevacizumab can accelerate the resolution of MHR-related macular edema and enhance the visual impact.[6,7] In addition, subtenon triamcinolone injection may also accelerate the resolution of subretinal and intraretinal fluid due to MHT.[11]

MHT presenting with severe ONL hemorrhage may benefit from intravitreal anti-VEGF, and in selected cases, intravitreal bevacizumab injections may serve as an adjunctive treatment for malignant hypertensive retinopathy; however, additional studies are needed to establish their safety and effectiveness.

Declaration of conflicting interests

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