Letters

OBSERVATION

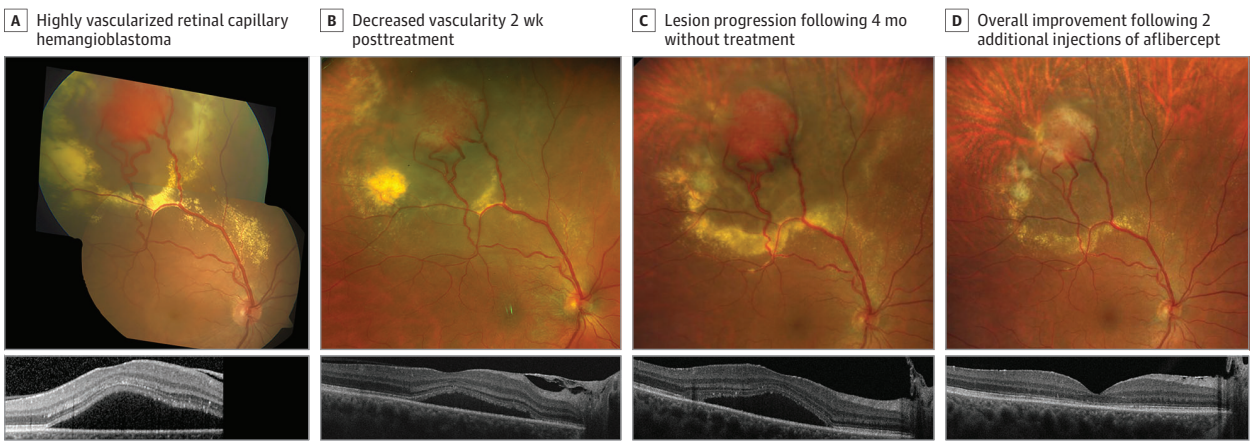
Assessment of Retinal Changes Following Intravitreal Aflibercept in 2 Patients With Von Hippel-Lindau Disease–Related Retinal Capillary Hemangioblastoma

Von Hippel-Lindau disease is a rare genetic disorder characterized by multiple benign and malignant neoplasms affecting multiple organ systems, including the retina. Laser photocoagulation, photodynamic therapy, and cryotherapy are options for ablating retinal capillary hemangioblastomas (RCHs).[1] Intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections using pegaptanib and ranibizumab have shown minimal effect on RCHs in lesion size and visual acuity (VA) with variable results on exudation.[2,3] We present 2 cases of peripheral RCHs associated with a series of aflibercept injections, highlighting its potential application as an adjunct treatment in this disease.

Report of Cases | *Case 1.* A 53-year-old male individual with Von Hippel-Lindau disease and a history of laser ablation for peripheral RCHs in the left eye at age 14 years presented for evaluation. His right eye had received intravitreal aflibercept 2 weeks prior in January 2021 without previous other treatment. VA measured 20/63 OD and 20/16 OS with current hyperopic correction of +1.25 in both eyes. The right eye had a large (approximately 3-disc diameter) lesion in the superotemporal periphery with tortuous, dilated feeding and draining vasculature, exudates, and subretinal fluid tracking inferiorly to the macula, which had improved compared with pretreatment (**Figure 1**A and B). Cryotherapy was planned, so aflibercept was continued to try to decrease macular edema and as prophylaxis for postcryotherapy exudation. Following 6 injections, exudation had improved and subfoveal subretinal fluid resolved, but a vascularized lesion persisted. Cryotherapy was postponed due to scheduling conflicts and the patient received no treatment for 4 months, during which time the lesion progressed, increasing in size, exudation, and vascularity (Figure 1C). After 2 additional aflibercept injections, his VA improved to 20/30 OD with resolution of macular exudation and subfoveal fluid and decreased lesion size, vascularity (both feeding and draining), and tortuosity (Figure 1D). Following a brief course of oral belzutifan, which was discontinued due to a pleural effusion, his most recent therapeutic plan includes continued aflibercept and possible laser or cryotherapy.

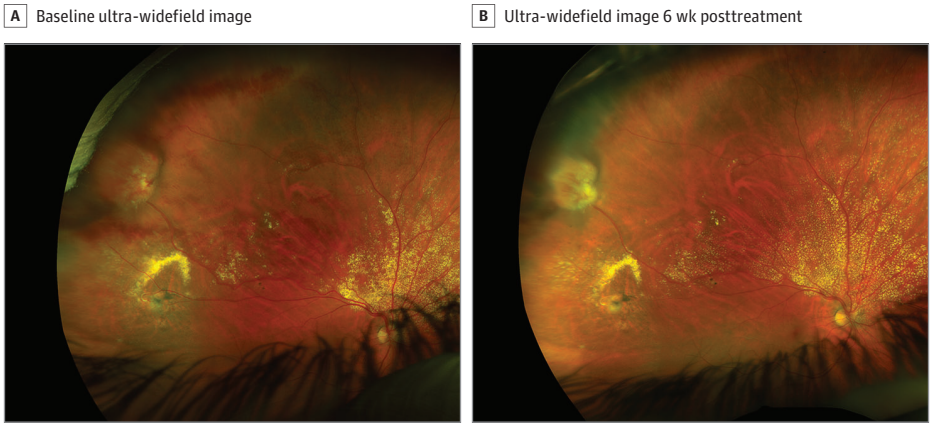
Case 2. A 38-year-old male individual with Von Hippel-Lindau disease and a history of laser ablation for small peripheral RCHs in both eyes presented with a large (approximately 4-disc diameter) treatment-naive RCH in the superotemporal far periphery in the right eye associated with preretinal hemorrhage and exudation not involving the macula (**Figure 2**A). He had VAs of 20/16 OD and 20/32 OS without correction. The tumor size combined with its peripheral location made it less amenable to laser, so cryotherapy was included in the treatment plan. Pretreatment with intravitreal aflibercept was initiated to try to provide some prophylaxis against postcryotherapy exudation. After the first aflibercept injection, the

Figure 1. Patient 1



Fundus images in color (top row of A, C, D) and pseudocolor (top row of B) and corresponding optical coherence tomography (bottom row) of patient 1. Prior to treatment, there is a highly vascularized retinal capillary hemangioblastoma in the superotemporal periphery with tortuous vasculature and peripheral lipid exudation extending inferiorly with subfoveal subretinal fluid (SRF; A). Two weeks after the first intravitreal aflibercept injection, decreased lesion vascularity, lipid exudation, and SRF are seen (B). Following a 4-month pause in aflibercept injections after the sixth injection, increased lesion size and exudation are seen. Intravitreal aflibercept was resumed and following 2 additional injections, montage color fundus photograph and corresponding optical coherence tomography show a more fibrotic, less vascularized retinal capillary hemangioblastoma with decreased feeding vessel caliber and tortuosity, improved peripheral lipid exudation, and resolved subfoveal SRF.

Figure 2. Patient 2



Baseline ultra-widefield image of patient 2 (A) showing the peripheral superotemporal retinal capillary hemangioblastoma with preretinal hemorrhage and dilated vasculature. Follow-up image 6 weeks after first aflibercept injection (B) reveals resolution of the preretinal hemorrhage, decrease in the lesion size and vessels, and a more fibrotic appearance.

lesion size and vascularity decreased (Figure 2B). He subsequently received a second aflibercept injection before undergoing cryotherapy with further lesion regression and preservation of his VA of 20/16 OD.

Discussion | These 2 cases of large, otherwise treatment-naive, active, peripheral RCHs associated with resolution of exudation following intravitreal aflibercept support a potential indication for anti-VEGF in general, and aflibercept specifically, to treat these lesions. Both lesions were associated with decreased size, vascularity, and exudation following intravitreal aflibercept. Mechanistically, ranibizumab, bevacizumab, pegaptanib, and brolucizumab target VEGF-A exclusively, while aflibercept also binds VEGF-B and placental growth factor[4] and faricimab also binds angiopoietin 2.

Intravitreal anti-VEGF in general, and aflibercept specifically, may be efficacious in treating RCHs, either as a monotherapy with serial injections or as an adjunct to permanent ablative treatments. In large lesions, which are particularly at risk of worsening exudation when treated with laser photocoagulation or cryotherapy alone,[1] pretreatment with aflibercept may have the potential to decrease the risk of macular exudation, allowing patients to potentially maintain VA while undergoing treatment.

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