CASE REPORT

Expression of angiogenic mediators in a patient with a retinal artery occlusion

The introduction of therapies targeting vascular endothelial growth factor (VEGF) has revolutionized the management of macular edema in the setting of ischemic retinal disease.[1–4] Recent evidence further supports a role for anti-VEGF therapy for the treatment of retinal neovascularization (NV) in diabetic patients.[5,6] These data have prompted clinicians to extend the use of anti-VEGF therapies for the treatment of retinal NV for other ischemic retinal diseases. However, emerging data support a role for additional angiogenic factors in the promotion of retinal NV in ischemic retinal disease.[7] Here we examine the expression of VEGF and other ischemia-driven angiogenic factors in the vitreous of a patient with an ischemic branch retinal artery occlusion (BRAO) who demonstrated progression of retinal NV despite treatment with scatter laser photocoagulation and anti-VEGF therapy.

Materials and Methods

Patient Samples

Institutional Review Board approval from the Johns Hopkins University School of Medicine was obtained for all patient samples used in this study. Vitreous samples were collected from consenting patients undergoing vitrectomy surgery at the Wilmer Eye Institute, and levels of VEGF, angiopoietin-like 4 (ANGPTL4), angiopoietin 2 (ANGPT2), and erythropoietin (EPO) protein were measured by enzyme-linked immunosorbent assay (ELISA)

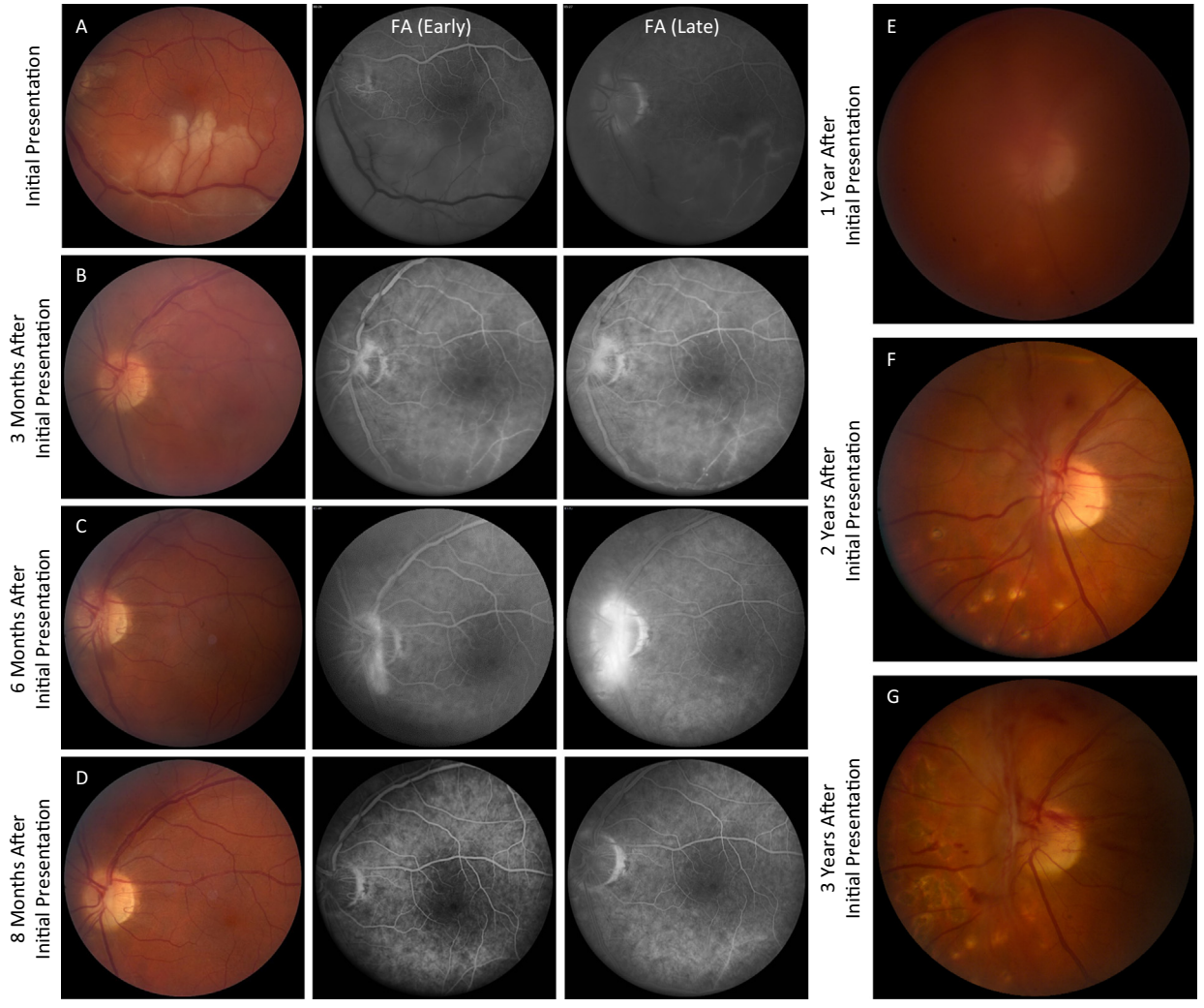

Fig. 1—Color fundus photographs and FA images chronicling clinical course of BRAO. (A) Color fundus photographs and FA images demonstrating BRAO in the left eye at initial presentation. Appearance (B) and progression (C) of disc neovascularization 3 and 6 months after initial presentation, respectively. (D) Regression of disc neovascularization after initiation of anti-VEGF therapy. (E) Return of disc neovascularization with associated VH despite sectoral laser photocoagulation. (F) Recurrent VH in the setting of disc neovascularization. (G) Increased disc neovascularization despite previous full pan-retinal laser photocoagulation treatment and anti-VEGF therapy. FA, fluorescein angiography; BRAO, branch retinal artery occlusion; VEGF, vascular endothelial growth factor; VH, vitreous hemorrhage.

(R&D Systems, Minneapolis, MN) for 5 nondiabetic controls, 5 proliferative diabetic retinopathy (PDR) patients, and our BRAO patient according to the manufacturer's protocols as previously described.[8]

Case Description

A 49-year-old male patient with a history of diabetes presented with decreased vision in his left eye. On examination, his visual acuity was 20/30 OU. Dilated examination demonstrated whitening of an inferotemporal artery in the left eye with surrounding retinal whitening, sparing the fovea. Fluorescein angiography (FA) images demonstrated reduced perfusion of the superotemporal arterial arcade and nonperfusion of the inferotemporal arterial arcade with delayed arterial-venous transit time (Fig. 1A). The patient was found to have BRAOs affecting the inferotemporal and superotemporal arcades without NV.

The patient returned 3 months later with new floaters in the affected eye. His vision had decreased to 20/50. Dilated examination demonstrated preretinal hemorrhage inferior to the inferotemporal arcade with NV of the disc (NVD), confirmed by FA (Fig. 1B). Sectoral scatter laser photocoagulation was performed to the ischemic retina. Three months later, the vitreous hemorrhage (VH) had resolved but the NVD had progressed (Fig. 1C). The sectoral scatter laser appeared adequate, and the patient received an intravitreal (IVT) injection with bevacizumab. The patient returned 2 months later and demonstrated regression of the NVD (Fig. 1D).

Four months later, 1 year after initial presentation, the patient returned and reported decreased vision over the prior month; his vision measured hand motion OU. The patient had a dense VH (Fig. 1E) and received a second IVT bevacizumab injection. The patient returned 3 weeks later with an improvement in vision (20/25), marked improvement of the VH, and regression of the NVD. Supplemental scatter laser was administered.

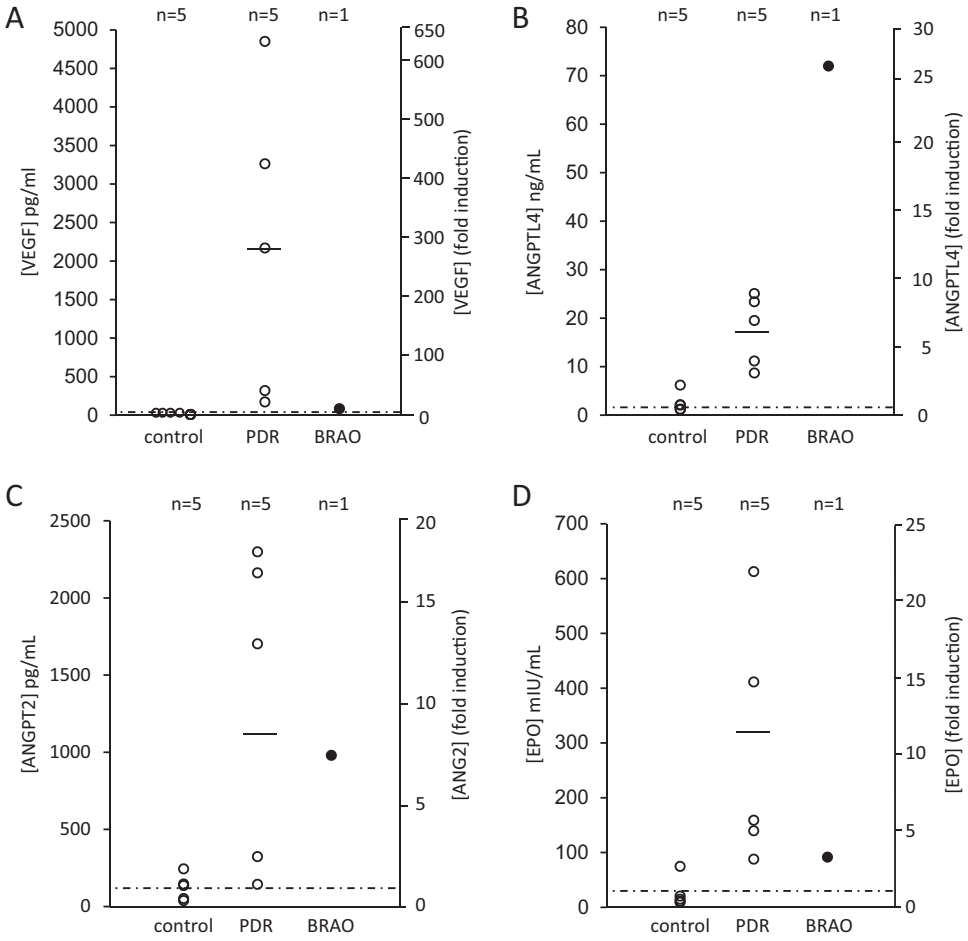

Fig. 2—Vitreous concentrations of VEGF, ANGPTL4, ANGPT2, and EPO in the BRAO patient compared with control or PDR patients. Vitreous concentrations of 4 known hypoxia-regulated angiogenic factors, VEGF (A), ANGPTL4 (B), ANGPT2 (C), and EPO (D), in the BRAO patient compared with nondiabetic control or PDR patients. Dotted line indicates average concentration for control patients. VEGF, vascular endothelial growth factor; ANGPTL4, angiopoietin-like 4; ANGPT2, angiopoietin 2; EPO, erythropoietin; BRAO, branch retinal artery occlusion.