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Case Report

Central Retinal Vein Occlusion Associated with Fibromuscular Dysplasia: A Case Report

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Anti-VEGF · Central retinal vein occlusion · Fibromuscular dysplasia · Hypertension

Abstract
In this report, we detail a rare presentation of central retinal vein occlusion (CRVO) in a patient with fibromuscular dysplasia (FMD). A 45-year-old woman with a 12-year history of FMD presented to the ophthalmology clinic with symptoms and exam findings consistent with CRVO. Dilated fundus examination revealed disc edema, diffuse flame, and dot-blot hemorrhages, and tortuous, engorged retinal veins. The patient was diagnosed with CRVO, and she was treated with monthly anti-VEGF monoclonal antibody followed by a VEGF inhibitor. At her most recent follow-up, her macular edema was resolved and her visual acuity had markedly improved. FMD has been shown to rarely present with retinal manifestations, especially in patients with hypertension. This appears to be first case report to document CRVO in the context of known FMD. We suggest that CRVO be considered as a potential complication for young patients with FMD.

Introduction

Fibromuscular dysplasia (FMD) is the proliferation of connective tissue and muscle fibers within arterial vessel walls typically in the medial layer, giving it its classic "string of beads" sign on angiography [1]. Nearly 90% of all documented cases of FMD have occurred in women,

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and the mean age of onset is 52 [2]. Small- and medium-sized arteries, including renal, carotid, and vertebral arteries, are most frequently affected by FMD. Involvement of the renal and carotid arteries can result in severe systemic hypertension therapy and carotid dissection, respectively [1]. While ocular manifestations of FMD are rare, central retinal artery occlusion (CRAO) has been reported [3, 4]. We present a case of central retinal vein occlusion (CRVO) in a patient with FMD. To our knowledge, this is the only reported case of this ocular complication in a patient with FMD.

Case Report

A 45-year-old woman with FMD and essential hypertension was referred to ophthalmology clinic for 3 weeks of decreased vision in her right eye. She was previously diagnosed with FMD after presenting to the emergency room 12 years prior with a headache and left-sided paresis and was found to have a right internal carotid dissection and right middle cerebral artery occlusion. A four-vessel arteriogram of the head demonstrated multifocal narrowing of the right vertebral artery consistent with a diagnosis of FMD. Renal ultrasound and MRA did not show involvement of the renal vasculature. Her severe hypertension was treated with an angiotensin-converting enzyme (ACE) inhibitor and monitored by her primary care provider. One week prior to presentation to ophthalmology, the patient was found to be mildly hypertensive to 144/80. Three weeks prior to presentation to our ophthalmology clinic, the patient had been seen by an outside provider who documented elevated intraocular pressure (IOP) of 34 mmHg and 26 mmHg in the right and left eyes, respectively. She was treated with brimonidine and referred to our clinic.

On examination at our clinic, the patient had best-corrected visual acuity of 20/60 in her right eye and 20/25 in her left with IOP of 15 mmHg and 13 mmHg in the right and left eyes, respectively. Extraocular movements and confrontational fields were normal. Pupillary response was sluggish, but no afferent pupillary defect was noted. Her anterior segment exam was normal. Dilated fundus exam of the right eye revealed disc edema, flame hemorrhages radiating from the optic disc extending into the midperiphery, diffuse dot-blot hemorrhages, and tortuous, engorged retinal veins (Fig.1). Fluorescein angiography identified delayed arterial filling and late optic disc staining (Fig.2). Optical coherence tomography (OCT) revealed intraretinal cysts and subretinal fluid with distortion of the foveal contour (Fig.3). Her left eye showed no evidence of retinopathy or abnormalities in fluorescein angiography or OCT.

The patient was diagnosed with CRVO and received intravitrealbevacizumab. Over the next year, the patient received monthly bevacizumab injections with resolution of her macular

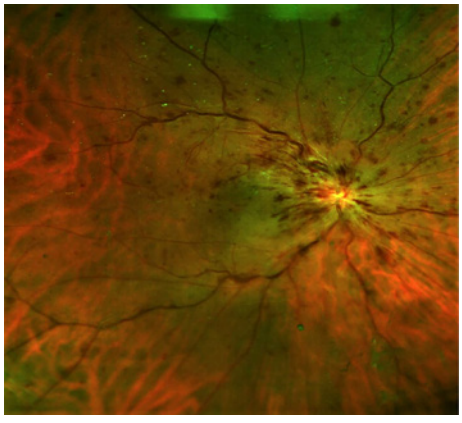

Fig. 1. Dilated fundus exam with disc edema, flame, and dot-blot hemorrhages radiating from the optic disc extending into the midperiphery, and tortuous, engorged retinal veins.

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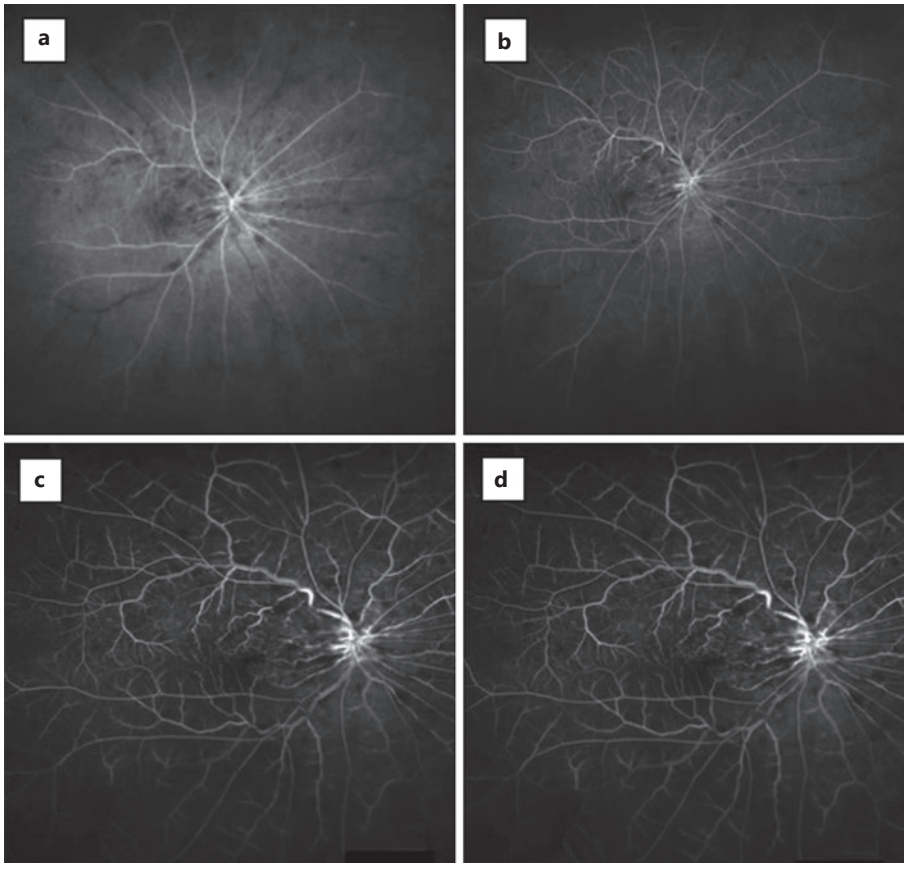

Fig. 2. Fluorescein angiography – (**a–b**) demonstrating delayed arterial filling at (44:14) and (52:07), respectively; (**c–d**) with dilated tortuous veins with blockage secondary to retinal hemorrhage pictured at (57:55) and (59:69), respectively.

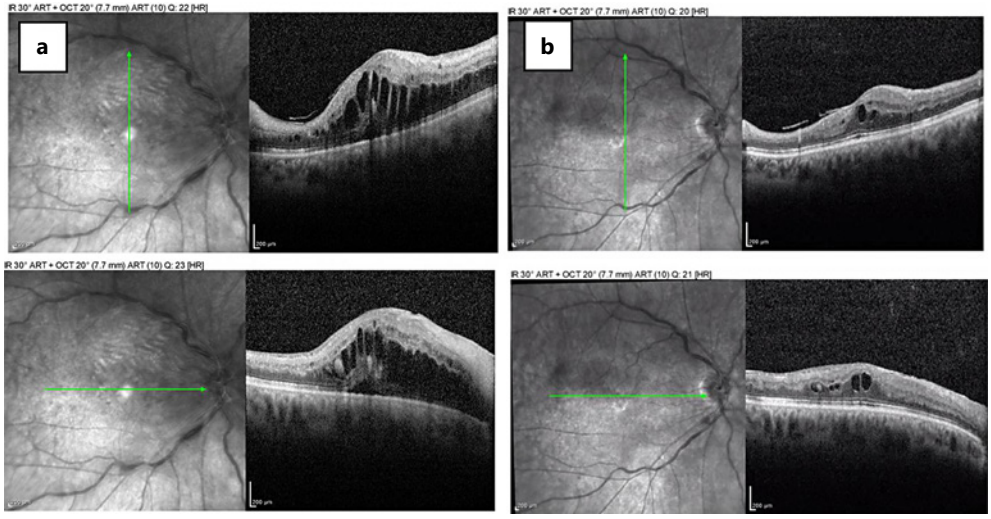

Fig. 3. a OCT of right eye on initial presentation demonstrating intraretinal cysts and subretinal fluid. **b** OCT of right eye upon follow-up after 1 year of treatment with intravitrealbevacizumab.

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edema and improvement of her vision to 20/40 in the right eye. She then chose to switch to aflibercept for ongoing therapy [5]. She was referred to a glaucoma specialist and started on latanoprost with adequate IOP control. Her primary care physician also reinitiated an ACE inhibitor for blood pressure control.

Discussion

CRVO is the second most common vascular disease of the retina leading to vision loss, trailing only diabetic retinopathy [6]. Risk factors for CRVO include age, hypertension, open-angle glaucoma, diabetes, hyperlipidemia, and hypercoagulable states [7]. CRVO is a condition that typically affects older adults, with a 4.6% prevalence among adults over the age of 80 and only a 0.7% prevalence among adults younger than 60 years of age [8]. Our patient was far younger than the average patient with CRVO; however, she did have a history of hypertension and FMD.

FMD has been reported to correlate with rare instances of CRAO [3, 4]. In at least two of the reported cases of CRAO in patients with FMD, renal involvement and hypertension were noted as contributory to the development of CRAO [4]. In such cases, management of hypertension is crucial to preventing pathology of retinal vasculature. In our case, the patient had a history of hypertension prior to diagnosis with FMD and her renal arteriogram was negative; thus, her hypertension was likely essential in nature rather than secondary to FMD. Her diagnosis of primary hypertension was further supported by negative serum and plasma studies for adrenal disease and a positive family history of early-onset hypertension.

The patient's hypertension was monitored by her primary care provider, and she was treated with an ACE inhibitor which she took inconsistently. In the week prior to her initial ophthalmology appointment, she was hypertensive to 144/88. This hypertension may have compounded with the direct effects of FMD on retinal vasculature to contribute to the patient's presentation. FMD has been associated with vascular changes throughout the body including the retinal vascular beds [4]. The central retinal vein passes through a common adventitial sheath alongside the central retinal artery. Thus, pathology of the central retinal artery, such as FMD, could result in compression and occlusion of the central retinal vein [9]. The patient's delayed arterial filling seen in fluorescein angiography may be indicative of fibromuscular changes of the retinal artery. However, this finding is also noted in several other case reports of acute CRVO without FMD and may be due to mild compression of the artery in the setting of venous occlusion and elevated IOP [10].

The patient's elevated IOP was also a likely contributing factor to the development of CRVO even though vascular compression is more commonly noted as the etiology of branch retinal vein occlusion rather than CRVO [9]. Another consideration is that thrombus formation may have contributed to the development of CRVO in this patient [11]. FMD has been shown to cause formation of venous thrombus in the femoral vein [12]. It is possible FMD of the retinal vasculature could create turbulent blood flow and promote thrombus formation and occlusion of the central retinal vein, especially in the setting of a patient who does not regularly take anti-hypertensive or anti-coagulant medication [13].

Complications of CRVO include vision loss, macular edema, and the development of neovascular glaucoma [7]. Of patients treated for CRVO, the majority of patients who present with visual acuity better than or equal to 20/40 are expected to have improved visual acuity over time. However, for the majority of patients with visual acuity between 20/50 and 20/200, the prognosis is often stabilization of visual acuity at that level [14]. In addition to baseline visual acuity, time to treatment with anti-VEGF therapy of less than

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30 days is predictive of better outcomes [15]. Case studies also demonstrate that for patients with CRVO and hypertension, anti-hypertensive medication is critical for the resolution and prevention of macular edema [16]. Fortunately, our patient had an excellent response to prompt anti-VEGF therapy with concurrent improvement in visual acuity and no long-term complications. She also responded well to re-initiation of anti-hypertensive therapy with an ACE inhibitor.

Early recognition and treatment of CRVO is important for preventing and minimizing complications and preserving eye function. FMD has been shown to rarely present with retinal manifestations, especially in patients with hypertension. Patients with FMD should seek treatment early for changes in vision. This case report demonstrates an example of a patient for whom FMD may have contributed to the development of CRVO.

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Statement of Ethics

The patient described in this report has given oral and written informed consent for publication of this medical case and its associated images. Reporting of this case is in compliance with the Declaration of Helsinki. The report does not include information that could identify the patient directly or indirectly. All medical interventions were delivered according to the latest protocols of treatment. The study protocol was reviewed, and the need for approval was waived by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Emma Astrike-Davis contributed to the conception and design of the manuscript. She was also involved in drafting and revising the final document. Daniel Olson also contributed to the conception and design of the manuscript and was involved in the drafting and revising of the final document. David Fleischman led the conception and design of the manuscript and provided critical review and revision of the final case report.

Data Availability Statement

All pertinent data evaluated in this case report are included in this article. For the purposes of patient privacy, additional data are not publicly available. Further inquiries can be directed to the corresponding author.

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