Hypertensive Scotomas in the Setting of Thrombotic Microangiopathy

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Abstract

Background:

- Malignant hypertension and thrombotic microangiopathy (TMA) represent overlapping microvascular pathologies that can also manifest as posterior polar ocular ischemia. This case highlights a concurrent pathology with reversible retinal findings following systemic stabilization.

Objective:

- To examine current literature and evidence in the management of malignant hypertension with concurrent acute-on-chronic thrombotic microangiopathy. This case exemplifies the aforementioned and may provide insight into future research and understanding of the pathophysiologic mechanisms at play in the posterior pole vasculature of the eye.

Introduction

- Malignant hypertension occurs more commonly in young adult African Americans than other populations.[1]
- Hypertensive retinopathy develops through arteriolar constriction, vascular occlusion, ischemia, and ultimately smooth muscle necrosis.[1]
- Malignant hypertension has multiple underlying systemic etiologies, including acute, chronic, and acute-on-chronic causes.
- Fundoscopic appearance of hypertensive emergency typically includes cotton wool spots (CWS), flame-shaped hemorrhages, fibrinous exudates, Elschnig spots, and macular edema.[2]
- Although peripapillary CWS are reported in literature with malignant hypertension, the marked focality and proximity around the optic nerve in the absence of other expected findings is unusual in this case.
- The peripapillary distribution is reflected by the high intravascular pressure placed on large arterioles near the optic disc which have not undergone pressure attenuation.[3]
- The ophthalmic manifestations of malignant hypertension fall into three histological categories; retinopathy, choroidopathy, and optic neuropathy as a result of the aforementioned.[1,2,6]
- Cotton wool spots were the primary finding on fundoscopic examination and, because they reflect focal ischemic injury via occlusion of terminal retinal arterioles with resultant axoplasmic stasis and swelling of the inner retinal nerve fiber layer, they warrant investigation for underlying vascular disease.[4]

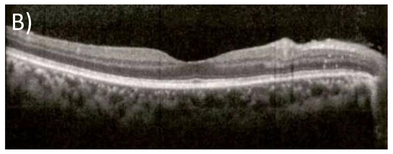

Figure 1.
A) Axonal report showing bilateral thickening of the retinal nerve fiber layer [RNFL] 4 days after symptom onset and significant following treatment 2 weeks later
B) OCT from the same scan showing associated retinal exudative changes extending to the macular region of the right eye

Clinical Course

Presentation:
A 31-year-old black female with PMH of anemia and gestational hypertension presented with a new onset of visual distortion right eye (OD) > left eye (OS) after developing hypertensive emergency.

- Four days prior, the patient presented to the emergency department for evaluation of outpatient abnormal labs, including elevated liver enzymes and creatinine.
- The patient subsequently developed hypertension up to 195/118 within 24 hours of being admitted to the hospital, requiring a nicardipine drip to lower her BP, after which she noticed vision changes starting the next day.
- Initial ophthalmology consultation revealed near vision of 20/40 (J2) OD and J1+ (20/20) OS. IOP 12 mmHg OD and 18 mmHg OS. No relevant afferent pupillary defect (rAPD) in both eyes (OU). Color vision reduced to test plate only OD and 8/8 OS. Extraocular movements were full. Confrontational visual field testing elucidated nasal and temporal scotomas bilaterally.
- Initial fundus examination revealed bilateral cotton wool spots (CWS) 360 degrees around both optic nerves, right eye more than left, but without optic nerve edema in either eye.
- One week later, the patient developed an rAPD in right the eye along with subtle optic nerve head edema.

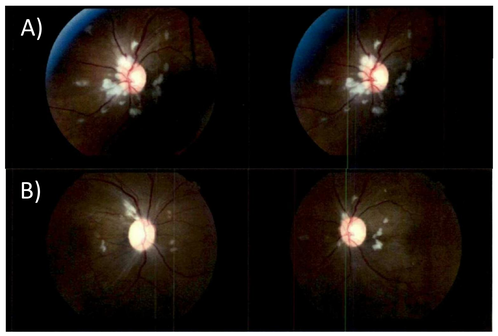

Figure 2.
A) Fundus photo taken four days after symptom onset showing multifocal peripapillary cotton wool spots (CWS).
B) Fundus photo taken three weeks later showing improvement in peripapillary CWS.

Workup:

- Lab work revealed elevated ESR, CRP, alpha-1 antitrypsin, and urine metanephrines, along with positive anti-smooth muscle and CMV IgG antibodies.
- Pertinent negatives: anti-AQP4, ANCA-MPO, ANCA-PR3, HIV 1/2, mitochondrial antibody, rheumatoid factor.
- OCT imaging four days after onset of vision changes revealed thickening of retinal nerve fiber layer and retinal exudative changes in both eyes (See figure 1A and 1B).
- MRI brain revealed nonspecific focal FLAIR abnormalities in the basal ganglia and pons.
- Echocardiogram revealed left ventricular hypertrophy with an ejection fraction of 45%.
- Carotid ultrasound was negative for stenosis bilaterally.
- Renal biopsy noted severe arteriolar sclerosis, widespread "onion-skin" lesions, and acute tubular injury with focal global glomerulosclerosis, suggesting acute-on-chronic TMA.

Methods and Materials

- A case report and literature review were both performed. Written consent was obtained from the patient.

Outcomes

Assessment: Transient scotomas secondary to hypertensive retinopathy in setting of acute on chronic thrombotic microangiopathic renal disease
Differential diagnosis: branch retinal artery occlusion, central retinal artery occlusion, diabetic retinopathy, Purtscher's traumatic angiopathy, and giant cell arteritis

Treatment:

- An oral steroid tapered course was started while inpatient following IV steroid administration.
- Goal-directed medical therapy for blood pressure control.
- Close follow up with interdisciplinary team including hematology, nephrology, neurology, and cardiology.
- Empiric eculizumab therapy was initiated outpatient for treatment of acute on chronic TMA.

Results:

- At 2-week follow up visit after discharge, visual scotomas were symptomatically improved, VAsc improved to 20/20 OU and color vision resolved to 8/8 fast in both eyes.
- On repeat dilated fundus exam, bilateral CWS were significantly reduced (Figure 2B).
- OCT revealed decreased bilateral optic nerve edema.
- Blood pressure better controlled with goal-directed medical therapy.

Discussion

- This 31-year-old female patient had a history of gestational hypertension, a known predisposing factor for the development of acute TMA.[1,5]
- Eculizumab is a pharmacologic agent that effectively binds and blocks factor C5 of the complement cascade.[5]
- Studies have shown > 50% of patients who develop TMA postpartum have identifiable complement mutations (a positive prognostic factor in treatment with eculizumab).[5]
- The large arterioles in the peripapillary area sustain the largest intravascular pressure in the posterior pole of the eye and attenuate across branching generations that extend towards the periphery.[3]
- The retinal peripapillary capillary plexus is the densest microvascular network in the posterior pole of the eye and runs parallel to the nerve fiber layer axons making the region more susceptible to damage in this setting.[8]
- The retinopathy with a peripapillary focus likely reflects the overlapping pathophysiology of both acute-on-chronic TMA and hypertensive vascular injury, as TMA-mediated endothelial injury may have preferentially amplified ischemia at the segment under the highest pressure load which, in this case, was the capillaries and arterioles directly extending from the optic disc.
- Following treatment, repeat fundus examination showed marked resolution of CWS, indicating recovery of retinal perfusion and effective systemic disease management.
- Further research on how these structures are differentially impacted by malignant hypertension in the setting of acute on chronic TMA may prove advantageous in understanding ocular vascular disease progression.

Conclusions

- This case underscores the importance of recognizing hypertensive retinopathy as a manifestation of systemic microangiopathic pathology. A comprehensive differential diagnosis coupled with prompt interdisciplinary evaluation is essential for identifying underlying systemic pathologies such as thrombotic microangiopathy.
- Early diagnosis and targeted systemic management are critical to optimizing both visual and systemic outcomes.

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