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Case report

Transient vision loss associated with paracentral acute middle maculopathy detected on multi-modal imaging

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ABSTRACT

Purpose: To report two patients with transient decreased vision and associated paracentral acute middle maculopathy (PAMM) lesions identified with multi-modal imaging, including what we believe to be the first documented patient of PAMM associated with iron deficiency anemia.

Observations: Case 1 is a 56-year-old man who experienced transient blurred vision one week following cardiac ablation for atrial fibrillation. Symptoms resolved by the time of presentation and visual acuity was 20/20 in each eye. Ocular examination was unremarkable aside from subtle discoloration within the papillomacular bundle in the right eye. Spectral domain optical coherence tomography (SD-OCT) revealed thickening of the middle retinal layers with a corresponding area of hyporeflectivity on the *en face* infrared image. This area of hyporeflectivity was confirmed on "structural" SD-OCT angiography, although no flow voids were identified. Fluorescein angiography was normal. Case 2 is a 25-year-old man with no past medical history who noted decreased central vision in his right eye upon awakening. Visual acuity was light perception in the right eye and 20/20 in the left eye. Posterior segment examination in the right eye showed tortuous retinal vessels and subtle pallor involving the superior part of the macula. SD-OCT showed thickening of the middle retinal layers of the superior macula with a corresponding area of hyporeflectivity on the *en face* infrared image. Systemic work-up was completed and identified severe iron deficiency anemia as the most likely inciting factor. In both cases, visual acuity was 20/20 in each eye at follow-up.

Conclusions: Small arterial occlusions of the retina remain difficult to diagnose and may represent a sequela of systemic disease. Multi-modal imaging is helpful in equivocal cases with subtle clinical findings.

Importance: The present case report illustrates the utility of multi-modal imaging in diagnosing transient ischemic events of the retina, and reports what we believe to be the first association of PAMM with iron deficiency anemia.

1. Introduction

Arterial occlusive disorders of the retina comprise a broad spectrum of disease. Visual outcomes vary and depend on multiple factors including the location of the occluded vessel and the time until reperfusion.[1,2] Advances in ophthalmic imaging, including spectral domain optical coherence tomography (SD-OCT) and optical coherence tomography angiography (OCT-A), have increased our ability to detect and diagnose arterial occlusions. However, transient occlusions can reperfuse prior to examination by an ophthalmologist making diagnosis more difficult. Here we present two relatively young patients with transient small vessel occlusions of the papillomacular bundle and associated paracentral acute middle maculopathy (PAMM) lesions in the setting of recent cardiac radio-frequency ablation and severe iron deficiency anemia.

2. Findings

2.1. Case 1

A 56-year-old man presented with blurred vision in the right eye that started one day prior and returned to baseline by the time of presentation. He denied any headache, scalp tenderness, or jaw claudication. Past medical history was significant for chronic atrial fibrillation for which he underwent radio-frequency ablation one week prior. Best corrected visual acuity was 20/20 in each eye. The examination was normal except for subtle thickening and pallor on the nasal side of the macula in the right eye.

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Multimodal retinal imaging was performed (Fig. 1). Wide-field fundus imaging (Optos, Dunfermline, UK) confirmed subtle changes in coloration within the papillomacular bundle of the right eye. SD-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) of the right eye showed thickening and diminished distinction between inner and middle retinal layers of the nasal macula, encroaching the fovea. Hyporeflectivity spatially corresponding to the area of abnormal thickening on OCT was appreciated on *en face* infrared imaging. SD-OCT angiography (OCT-A) (AngioPlex, Zeiss, Oberkochen, Germany) showed the area of hyporeflectivity on the "structural" image but did not show any signal flow voids (Fig. 2). Fluorescein angiography was essentially normal, although there was questionable staining of an arteriole exiting the temporal aspect of the optic disc (Fig. 1B, yellow arrow). A more sensitive swept-source OCT-A (SS-OCTA) was not available at the time of examination. A re-perfused small arterial occlusion within the papillomacular bundle was suspected and the patient underwent subsequent inpatient evaluation to rule out stroke. All cardiac studies were negative.

At one month follow-up, the patient reported continued improvement in symptoms. Best corrected visual acuity was again 20/20 in each eye. SD-OCT revealed almost complete reconstitution of the middle retinal layer boundaries and normal retinal thickness. *En face* infrared imaging showed a near normal papillomacular bundle, with a barely perceptible difference in reflectivity between the area of pathology and surrounding normal retina. OCT-A was again normal.

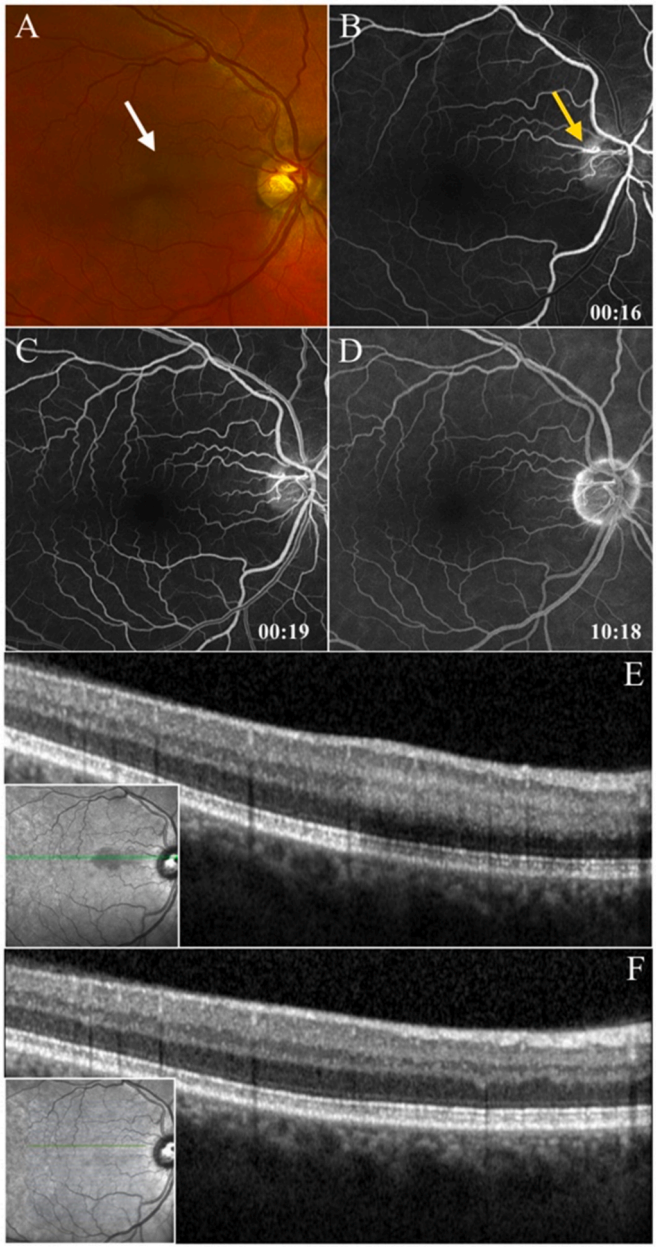

Fig. 1. Multi-modal imaging of a PAMM lesion following cardiac ablation. (A) Color fundus photography of the right eye. Note subtle white discoloration nasal to the fovea of the right eye (white arrow). (B–D) Fluorescein angiography of the right eye during the arterial (B), venous laminar (C), and late venous phase (D). Questionable staining of a small vessel exiting the optic disc is seen in the early frames (yellow arrow). No obvious ischemia is apparent. (E) *En face* infrared imaging (inset) and corresponding SD-OCT through the lesion noted in the right macula. Note the thickening and decreased distinction between the middle and inner retinal layers (white arrow). (F) *En face* infared imaging (inset) and corresponding SD-OCT at one month follow-up. Note the normalization of infrared reflectivity and improvement of middle retinal layer distortion compared to initial visit. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

2.2. Case 2

A 24-year-old man presented with complaint of acute loss of central vision in the right eye which he noticed upon awakening. He denied any past cardiovascular or ocular history, recent changes to his health, or trauma. Visual acuity was light perception with noted poor effort in the

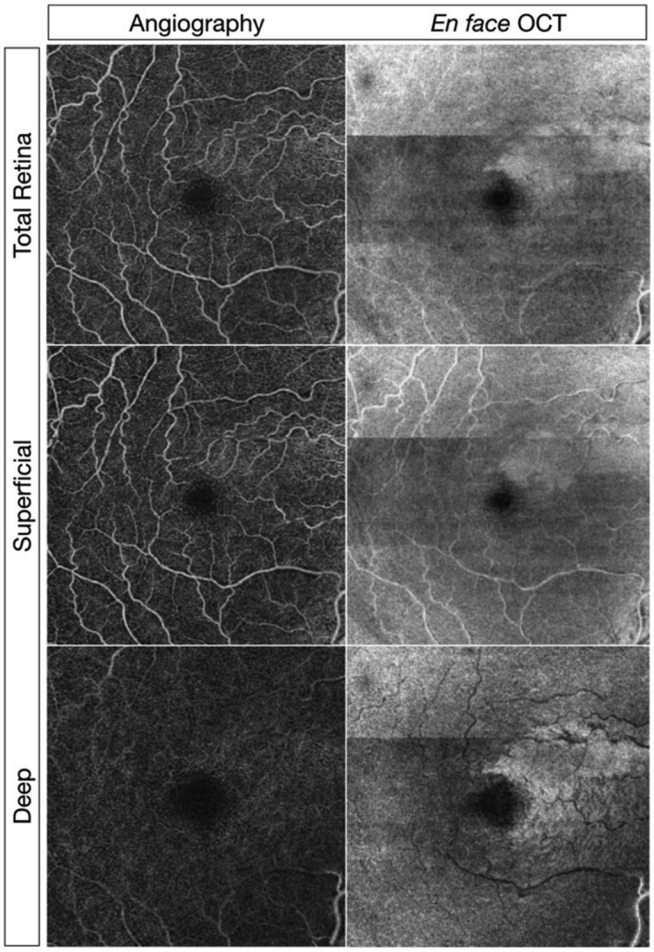

Fig. 2. Spectral domain optical coherence tomography angiography (SD-OCT-A) imaging. Representative slabs illustrating OCT-angiography (first column) of total (first row), superficial (second row), and deep (third row) retina vessels which appear normal with no flow voids. Corresponding *en face* structural OCT (second column) revealing abnormal reflectivity in the area of the suspected small vessel occlusion, similar to that seen on the *en face* infrared image.

right eye and 20/30 in the left eye. Ocular examination was notable for tortuous retinal veins and a pale superior macula in the right eye. The left eye was normal. Multimodal retinal imaging was unable to be performed on the day of presentation, but was completed four days later (Fig. 3). Wide-field fundus imaging (Optos) confirmed exam findings. SD-OCT of the right eye showed thickening and diminished distinction between inner and middle retinal layers of the superonasal macula. Hyporeflectivity spatially corresponding to the area of abnormal thickening on OCT was appreciated on *en face* infrared imaging. Fluorescein angiography was normal. OCT-A was not performed.

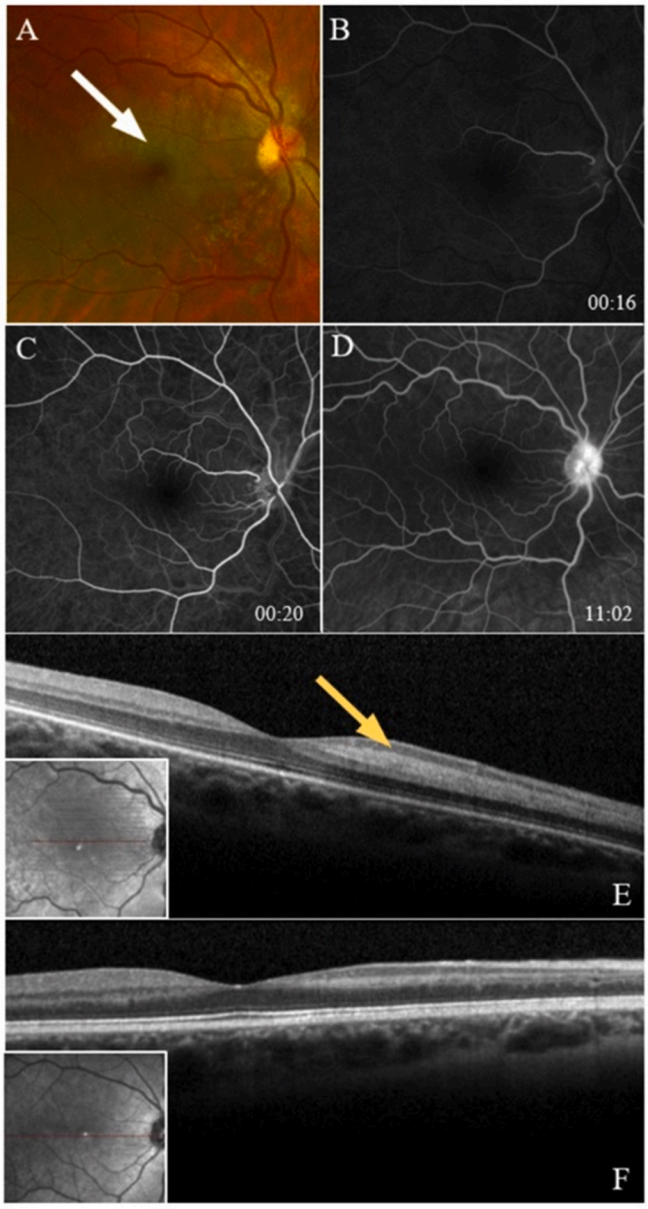

Fig. 3. Multi-modal imaging of a PAMM lesion in a patient with severe iron deficiency anemia. (A) Color fundus photography of the right eye. Note white discoloration superonasal to the fovea of the right eye (white arrow). (B–D) Fluorescein angiography of the right eye during the arterial (B), venous laminar (C), and late venous phase (D) showing vascular tortuosity without any delayed filling four days after presentation. (E) *En face* infrared imaging (inset) and corresponding SD-OCT through the lesion noted in the right macula. Note the thickening and decreased distinction between the middle and inner retinal layers (yellow arrow). (F) *En face* infared imaging (inset) and corresponding SD-OCT at one month follow-up. Note the improved infrared reflectivity and improving middle retinal layer thickening and distortion at follow-up. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

The patient was referred for inpatient work-up to rule out stroke. Neuroimaging was normal and an extensive laboratory work-up was negative for infectious and inflammatory etiologies. A hypercoagulable work-up was also negative. However, the patient was found to have severe iron deficiency anemia with notable findings of low hemoglobin (8.0g/dL), low mean red blood cell corpuscular volume (77.5 fL), low serum ferritin (6 ng/mL), low serum iron (<10 mcg/dL), low transferrin saturation (2.7%), and marked compensatory reticulocytosis (117,160 cells/uL). His anemia improved with supplemental ferrous sulfate, however an etiology for iron deficiency was not elucidated. Of note, a sickle cell disease screening test was negative. Gastrointestinal evaluation via esophagogastroduodenoscopy, colonoscopy, and capsule endoscopy revealed external hemorrhoids that were not felt to correlate to the extent of iron deficiency anemia. At follow-up one month later, his vision subjectively improved back to baseline best corrected visual acuity of 20/20 in the affected eye.

3. Discussion

Retinal vascular occlusions, including of the cilioretinal artery, can cause permanent or transient changes in the retina. Long-term visual outcomes are variable but generally more favorable with transient occlusions.[3] Hayreh et al. reported 100% of "transient" BRAOs achieved better than 20/40 vision, as opposed to 89% of "permanent" BRAOs.[1] Transient retinal ischemia was suspected in both patients based on exam and SD-OCT imaging findings, despite no obvious perfusion defect on fluorescein angiography. At the time of initial imaging, normal blood flow likely resumed and the lesions were therefore undetectable on FA and OCT-A. Similar to the aforementioned studies, final visual acuity for both cases was favorable and returned to baseline.

Both patients demonstrated OCT findings consistent with paracentral acute middle maculopathy (PAMM), which was first described in 2013 by Sarraf et al. and is a descriptor for a characteristic OCT pattern in patients with likely retinal capillary ischemia.[4] In the acute phase, PAMM appears as a placoid-like lesion, often with subtle pallor on exam, and corresponding hyperreflectivity on OCT within the inner nuclear layer, but not extending to photoreceptors.[5,6] The etiology of PAMM remains unknown. Although it is most often described in the context of primary retinal vascular disorders,[6] other systemic conditions are associated which include diabetes mellitus, blood dycrasias, hypercoaguable states (i.e, pregnancy),[7,8] and medication side effects (i.e phosphodiesterase-5 inhibitors).[9] PAMM is also reported following ocular surgery and trauma.[10–12] Other theories suggest a possible role of environmental exposures, such as caffeine and oral contraceptives, but a definitive relationship is not yet established.

The first patient exhibited retinal ischemia in the context of a recent cardiac ablative procedure. An association between atrial fibrillation (AF) and vascular occlusive disease is well documented, with a strong link to ischemic stroke.[13–15] A recent metanalysis reported a prevalence of atrial fibrillation in 4.1–21.4% of patients with retinal artery or vein occlusions.[16] Although increased risk of thromboembolism in the early perioperative period of cardiac ablation is well-documented,[17] we were unable to find reports of PAMM or retinal artery occlusion shortly after ablation.

The likely etiology for our second case was more elusive. A systemic work-up was largely negative, however the patient had severe iron-deficiency anemia. PAMM is reported in association with hematologic diseases, such as hemolytic uremic syndrome and sickle cell disease which inherently yield an increased risk of systemic thrombosis.[18,19] We believe that this represents the first reported case of PAMM associated with iron deficiency anemia. It is possible that additional risk factors not elicited upon history were also present as a 'second hit'. In young patients, it is especially important to inquire about risk factors such as dehydration, recreational drug use, trauma, or other high risk behaviors

- of which our patient denied.

4. Conclusions

In patients with vision loss associated with PAMM, more than one imaging modality may be helpful in establishing the diagnosis as retinal blood flow can be normal at the time of initial evaluation. A high index of suspicion should be maintained in patients with risk factors for vascular occlusive disease and equivocal or subtle exam findings.

Patient consent

Written consent was obtained from both patients prior to submission for publication.

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Authorship

All authors attest that the meet the current ICMJE criteria for authorship.

Authors' contributions

JDS, LZ, JS, HWF, and SGS interpreted patient data and wrote the manuscript.

Declaration of competing interest

The following authors have no financial disclosures: JDS, LZ, JS, HWF, SGS.

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