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Branch retinal artery occlusion in a 49-year-Old woman taking phentermine

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ABSTRACT

Purpose: This report describes the presentation of a 49-year-old woman with a branch retinal artery occlusion of the right eye in the setting of taking phentermine, a commonly used weight loss medication.

Observations: A 49-year-old woman presented with acute painless vision loss in her right eye and was found to have a branch retinal artery occlusion after taking prescribed dosages of phentermine for weight loss therapy. Fundus examination revealed retinal whitening in the distribution of the superior temporal branch retinal artery, and spectral domain optical coherence tomography demonstrated macular edema. Systemic evaluation was negative for cardiovascular, infectious, or autoimmune etiologies. Based on the retinal findings, the patient was diagnosed with phentermine associated branch retinal artery occlusion. She was followed for nine years with no further complications and her vision remained stable in the right eye.

Conclusions and Importance: This case highlights that phentermine, a commonly used weight loss medication, could be associated with ischemic retinopathies. Thus, clinicians should be aware that retinal vascular occlusions may not only occur in those who use recreational amphetamines but also in patients taking the prescribed dosages of a weight loss medication like phentermine.

1. Introduction

Phentermine is an amphetamine-like sympathomimetic drug that the Food and Drug Administration (FDA) approved as a short-term (up to 12 weeks) weight loss therapy.[1,2] While studies have shown that this drug is safe, several case reports have demonstrated phentermine being associated with adverse effects including stroke, myocardial infarction, and ischemic ocular diseases.[3–8] In addition, other amphetamine derivatives, especially ones that are abused like methamphetamine and cocaine, have been well documented to have harmful effects on the cardiovascular, neurologic, and psychologic systems.[9] In particular, ocular side effects of amphetamine abuse include mydriasis, decreased accommodation and convergence, visual hallucinations, retinal vasoconstriction and vasculitis, retinal microaneurysms and hemorrhage, and anterior ischemic optic neuropathy.[6,10–13] To date, there have been few studies reporting on the ocular effects of phentermine, especially on the retinal vasculature. Herein, we report a case of a patient with no significant past medical history presenting with a branch retinal artery occlusion (BRAO) after taking prescribed dosages of phentermine.

2. Case report

A 49-year-old woman presented to the emergency department with acute painless vision loss in her right eye. She had no significant medical history including heart disease, diabetes mellitus, hypertension, hypercholesterolemia, or stroke. Her body mass index (BMI) was 27.4 kg/m^2. She was taking 37.5 mg of phentermine once daily for two months for weight loss therapy and was not on any other medications or supplements. Best-corrected visual acuity (BCVA) was 20/20 in both eyes. The pupils were round and reactive to light. Intraocular pressures were unremarkable in both eyes. Extraocular motility was unremarkable. Visual field examination of the right eye revealed an inferior defect. Slit-lamp examination was unremarkable. Dilated fundus examination of the right eye showed retinal whitening in the distribution of the superior temporal branch retinal artery while the left eye was unremarkable (Fig. 1). Spectral domain optical coherence tomography (SD-OCT) imaging (Cirrus, Carl Zeiss Meditec, Dublin, CA) revealed retinal edema superior to the fovea in the right eye while the left eye was unremarkable (Fig. 2).

To identify possible causation of the BRAO, the patient underwent

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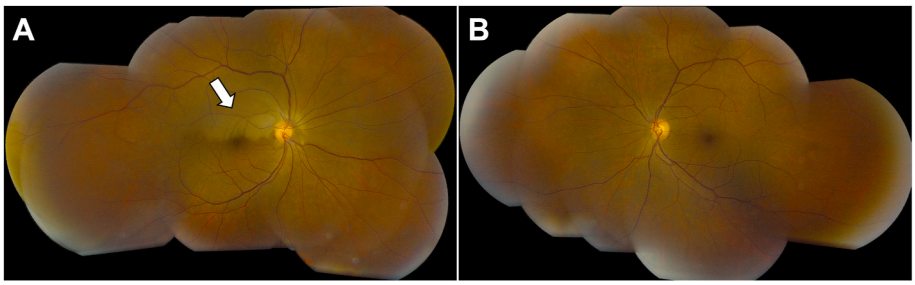

Fig. 1. Montage color fundus photographs (CFPs) of the right and left eye of a 49-year-old woman with a branch retinal artery occlusion in the right eye at the initial visit. **A)** Montage CFP of the right eye showing retinal whitening in the distribution of a branch retinal artery superior to the fovea (white arrow). **B)** Montage CFP of the unremarkable left eye.

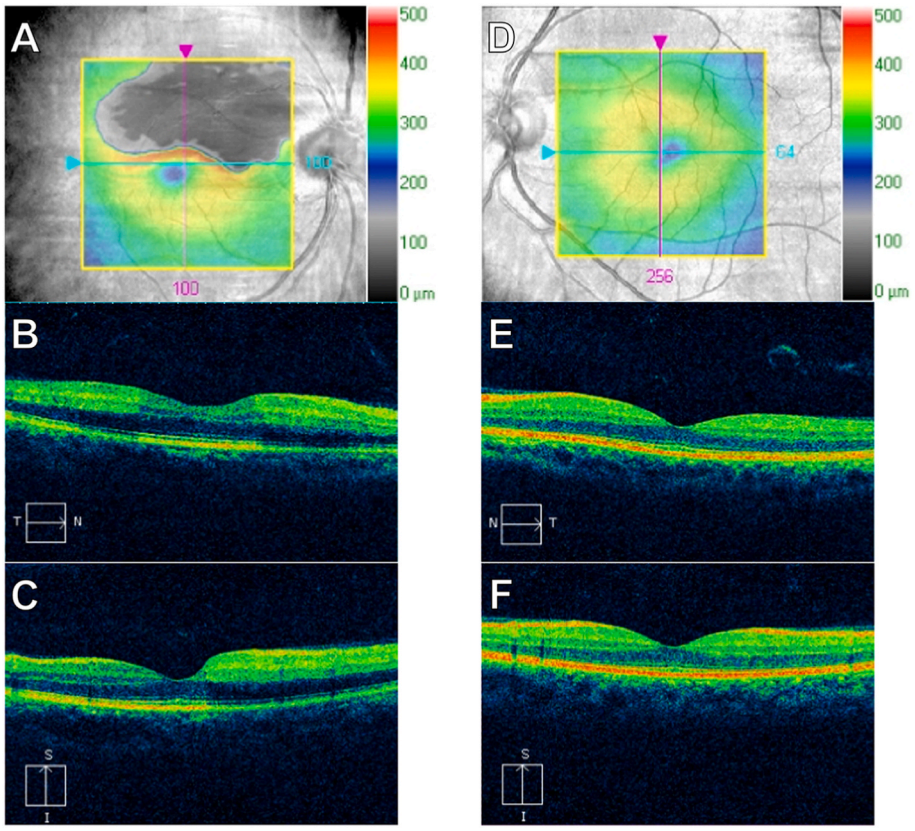

Fig. 2. Spectral domain optical coherence tomography (SD-OCT) images of the patient's right and left eye at the initial visit. **A-C)** *En face* macular thickness map and B-scans of the patient's right eye. The *en face* macular thickness map (**A**) shows a gray area superior to the fovea that corresponds to the region of the branch retinal artery occlusion (BRAO). However, the segmentation fails due to the edema in the inner retinal layer. The horizontal (**B**) and vertical (**C**) B-scans show a thickened inner retina in the superior macular secondary to the BRAO. **D-F)** *En face* macular thickness map and B-scans of the patient's left eye. The *en face* macular thickness map (**D**) as well as horizontal (**E**) and vertical (**F**) B-scans are unremarkable.

related systems examinations. The review of systems was unremarkable. Carotid duplex ultrasound as well as transthoracic and transesophageal echocardiogram were unremarkable with an ejection fraction of 60%. Laboratory results including complete blood count, erythrocyte sedimentation rate, c-reactive protein, coagulation function, and angiotensin converting enzyme levels were within normal limits. In addition, antinuclear antibody, anticardiolipin antibody, Toxoplasma gondii antibodies, and fluorescent treponemal antibodies were negative.

The patient was diagnosed with phentermine associated BRAO and was instructed to discontinue the medication immediately. She was followed for the next nine years with no further complications. Her BCVA remained stable at 20/20 in both eyes. Her inferior visual field defect in the right eye remained with the patient making lifestyle adjustments to accommodate for the defect. Swept-source OCT angiography (SS-OCTA) imaging (PLEX® Elite 9000, Carl Zeiss Meditec, Dublin, CA) in the right eye at the last follow-up visit showed an area of non-perfusion in the superficial retina superior to the fovea and is in the same location as the BRAO seen at the first visit (Fig. 3).

3. Discussion

Phentermine is a sympathomimetic amine with pharmacological activity similar to amphetamines. It has been approved by the FDA since 1959 for short-term use in combination with a regimen of weight reduction-based exercise, behavioral modification, and caloric restriction in the management of obesity for patients with an initial BMI greater than or equal to 30 kg/m^2.[2] However, there are limited efficacy and safety data on this drug and few studies have looked at the long-term

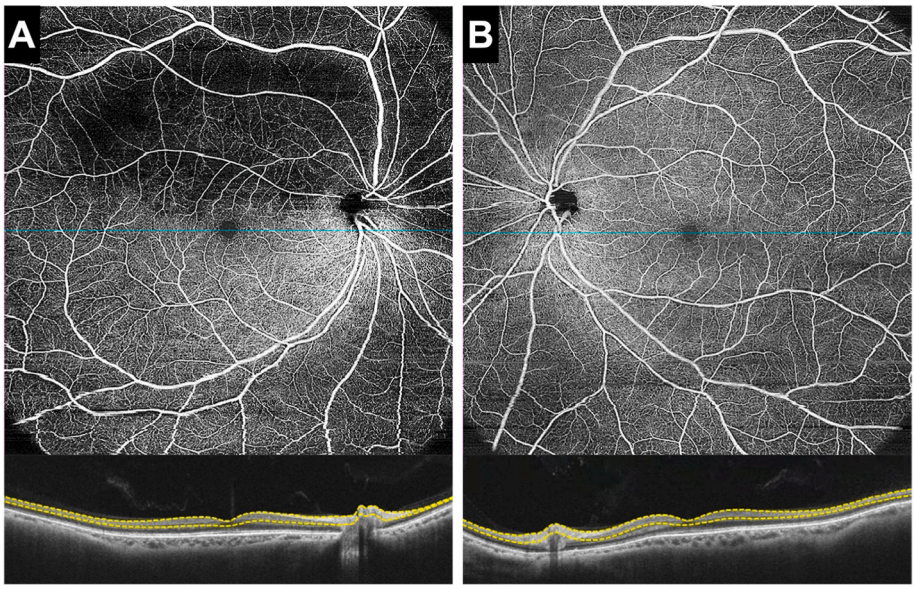

Fig. 3. *En face* swept-source optical coherence tomography angiography (SS-OCTA) of the right and left eye at the last follow-up visit. The 15 × 15 mm SS-OCTA images were created using a superficial retinal slab. **A)** *En face* SS-OCTA image and B-scan of the right eye showing an area of non-perfusion in the superficial retina along the distribution of the superior temporal branch retinal artery. **B)** *En face* SS-OCTA image and B-scan of the left eye revealing normal perfusion of the superficial retina.

effects.[14] Phentermine mainly acts on the central nervous system as a norepinephrine reuptake inhibitor, which results in suppressing appetite.[2] It was initially marketed as "Fen-Phen", which was a compound of fenfluramine and phentermine. However, in 1997, this medication was taken off the market because of concerns of increased risk for valvular heart disease, which was thought to be mainly due to fenfluramine.[5,15,16] Thus, phentermine monotherapy has continued to be used today and is one of the most commonly prescribed drugs for weight loss treatment.[17]

Even though studies have shown that phentermine is safe for short-term use and does not have significant adverse effects, there have been several case reports describing the association of phentermine with vascular diseases including stroke and myocardial infarction.[3–5] These reports concluded that phentermine's sympathetic properties can cause vasoconstriction and vasospasm leading to ischemia in different organ systems. Chan[6] reported a 35-year-old woman who developed an acute non-arteritic anterior ischemic optic neuropathy (NAION) after taking two prescribed dosages of phentermine. Consequently, he concluded that the patient's vision loss was due to vasoconstriction of the posterior ciliary arteries secondary to phentermine use. In addition, Cho et al.[7] and Huh et al.[8] reported on patients who presented with a central retinal vein occlusion (CRVO) after taking prescribed dosages of phendimetrazine, another sympathomimetic amine used as an appetite suppressant. As a result, based on these case reports, sympathomimetic amines like phentermine may have an adverse physiological effect on the retinal vasculature.

Since phentermine is structurally and pharmacologically related to amphetamines, it is reasonable to conclude that both drugs could have similar adverse effects. In particular, many studies have shown that methamphetamine can cause ocular disorders, particularly retinal vascular events like central retinal artery occlusions, intraretinal hemorrhage, and retinal vasculitis.[13,18,19] These retinal vascular disorders are likely due to the sympathomimetic effects of methamphetamine, which may induce extensive vasoconstriction and vasospasm.[10–12]

In this report, we described a patient with no significant past medical history presenting with a unilateral BRAO after taking prescribed dosages of phentermine. Based on prior studies and case reports, we speculate that phentermine caused extensive vasoconstriction or vasospasm of a branch retinal artery, which led to the development of the BRAO in our patient. This is consistent with other case reports associating sympathomimetic amines used for weight loss therapy with ischemic events like stroke, myocardial infarction, acute NAION, and CRVO. Thus, the purpose of this report is to add to the current literature and make providers more aware of the ocular adverse effects of this weight loss medication.

4. Conclusions

In summary, we report a case of a patient presenting with a BRAO after taking prescribed dosages of phentermine and emphasize the possible ocular adverse effects of this weight loss medication. As a result, it is important to be aware that retinal vascular occlusions may not only occur in patients using recreational amphetamines but also in those taking the prescribed dosages of commonly used medications like phentermine.

5. Declaration

After conducting a literature review on September 1, 2023, utilizing PubMed, Google Scholar, and ResearchGate using the key words phentermine, branch retinal artery occlusion, central retinal artery occlusion, methamphetamine, amphetamine, ischemic retinopathy, and retinal vascular occlusions, we did not find any prior reports documenting the association between phentermine and branch retinal artery occlusion.

6. Patient consent

Written informed consent was obtained from the patient for the publication of this case report. All procedures were performed in accordance with the tenets of the Declaration of Helskinki and complied with the Health Insurance Portability and Accountability Act of 1996.

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Conflict of interest

Philip J. Rosenfeld received research support from Carl Zeiss Meditec, Inc. He also received research funding from Gyroscope Therapeutics and Stealth BioTherapeutics. He is also a consultant for Apellis, Boehringer-Ingelheim, Carl Zeiss Meditec, Chengdu Kanghong Biotech, InflammX/Ocunexus Therapeutics, Ocudyne, Regeneron Pharmaceuticals, and Unity Biotechnology. He also has equity interest in Apellis, Valitor, and Ocudyne.

The following authors have no financial disclosures: JL and SRD.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Jeremy Liu: Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Philip J. Rosenfeld:** Investigation, Project administration, Resources, Writing – original draft. **Sander R. Dubovy:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Potential conflict of interest exists: We wish to draw the attention of the Editor to the following facts, which may be considered as potential conflicts of interest, and to significant financial contributions to this work:

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