CENTRAL RETINAL VEIN OCCLUSION ASSOCIATED WITH USE OF AMYL NITRITE "POPPERS"

Andrew Lam, MD, Shilpa Gulati, MD, Bradley S. Foster, MD, David R. Lally, MD

Purpose: To report a case of central retinal vein occlusion in a young patient after the use of amyl nitrate "poppers."

Methods: Description of the patient's clinical history, ophthalmic examination, retinal imaging, and treatment.

Results: A 38-year-old man presented with a central retinal vein occlusion in his right eye after inhaling amyl nitrite "poppers." There appeared to be a definitive temporal association between poppers use and both the onset of the vein occlusion and the patient's visual scotomata, which recurred immediately after drug use multiple times. Optical coherence tomography displayed cystic macular edema, which was treated with intravitreal bevacizumab. The patient's hypercoagulable laboratory workup was negative.

Conclusion: This is the first report of a central retinal vein occlusion associated with poppers inhalation. A high index of suspicion for poppers use should be maintained in young patients who present with retinal vein occlusion, particularly in homosexual patients with a normal laboratory workup that fails to reveal a hypercoagulable etiology.

RETINAL CASES & BRIEF REPORTS 18:138–140, 2024

From the Department of Ophthalmology, University of Massachusetts Medical School, Springfield, Massachusetts.

"Poppers" is a slang term given to a group of recreational drugs containing alkyl nitrite compounds that are used to enhance sexual arousal and for their myorelaxant effects. The name "poppers" originated from a common manner of commercial packaging in which users break, or "pop," a capsule before inhaling its contents through the nose. In June 2021, the U.S. Food and Drug Administration issued a warning to inform the public of increasing reports of hospitalizations and deaths associated with ingestion of nitrite poppers.[1] Amyl nitrite, the most popular inhaled form of the drug, is commonly sold online by manufacturers that package and label their products to appear safe, similar to energy drinks. Poppers have been previously associated with a form of maculopathy with clinical signs similar to photic injury and characterized by yellow foveal spots resulting from outer retinal changes.[2] Here, we report a patient whose popper use appears to have induced a central retinal vein occlusion.

None of the authors has any financial/conflicting interests to disclose.

Reprint requests: Andrew Lam, MD, New England Retina Consultants, P.C., 3640 Main Street, Suite 201, Springfield, MA 01107; e-mail: Andrew.Lam@aya.yale.edu

Case Report

A thirty-eight-year-old man presented after recently inhaling amyl nitrite poppers four times within one week. He had not previously used the drug and did not use any other recreational drugs concomitantly. After each use, he experienced a "yellow" scotoma centrally in his right eye only. With each episode, he promptly went to bed, and the first three times, the scotoma was gone in the morning. The fourth time, the scotoma persisted. He was referred for retina evaluation 2 weeks later.

The patient was otherwise healthy and had no other significant medical history. His vision, with correction, was 20/25 in each eye. Pupils, confrontation visual fields, eye pressure, and extraocular movements were all within normal limits. Slit-lamp examination of the anterior segment was unremarkable in both eyes. Funduscopic examination revealed dilated and tortuous veins, retinal hemorrhages, and optic nerve edema consistent with a central retinal vein occlusion in the right eye (Figure 1). The left fundus was normal. The classic yellow, subfoveal spots characteristic of "poppers" maculopathy was not seen in either eye.

Fluorescein angiography revealed papillophlebitis typical of central retinal vein occlusion in a young patient, with optic disc and perivenular leakage in the right eye, and without capillary nonperfusion (Figure 2). The left eye did not display any leakage

Fig. 1. Color fundus photograph showing blurred and elevated optic nerve margins, engorged and tortuous retinal veins, and hemorrhages in the macula and all quadrants of the periphery.

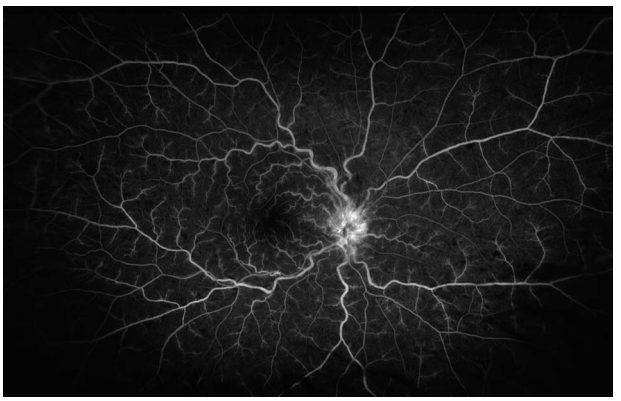

Fig. 2. Fluorescein angiogram of the right eye notable for optic disc leakage, and staining and diffuse leakage of retinal veins.

on angiography. Optical coherence tomography showed mild cystic macular edema in the right eye without disruption of the photoreceptors at the fovea; there was no optical coherence tomography evidence of poppers maculopathy (Figure 3).

The patient was traveling from another state and he chose to be seen by another retina specialist near his home. At this visit, approximately one month later, his vision in the right eye was 20/40 and his macular edema had worsened. He was treated with intravitreal bevacizumab. He also saw his primary care doctor who ordered the requested hypercoagulable laboratory workup. The following tests were all within normal limits, negative, or non-reactive: complete blood count, homocysteine, Factor V Leiden, PT/PTT/INR, protein C & S, anticardiolipin antibody, lupus anticoagulant, C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor, rapid plasma reagin (RPR), quantiFERON-TB Gold, and HIV. An antinuclear antibody test was initially weakly positive but then negative upon repeat testing.

One week after his bevacizumab injection, the patient traveled back to our area and was reexamined at our office. The vision in his right eye had improved to 20/25 with resolution of his central scotoma. The optical coherence tomography scan of the right macula displayed normal central macular thickness with no cystic edema or evidence of poppers maculopathy.

Discussion

"Poppers maculopathy" is a condition associated with amyl nitrite use that has been reported by numerous authors since first described in 2004.[3] This is the first report of a possible association between poppers use and a central retinal vein occlusion in a young patient. Amyl nitrite is a well-known vasodilator that affects both the arterial and venous circulations and has been historically used to alleviate symptoms of angina.[4] The pathophysiology most likely to predispose young patients to vein occlusion stems from venous vasodilation and blood pressure reduction that slows blood flow, encourages stasis, and promotes thrombus formation. The dilatory effect of amyl nitrite is believed to be due to direct action of nitric oxide on vascular smooth muscle.[5] It is possible that repeated use of poppers within a short time frame exacerbated this patient's degree of venous stasis and augmented his likelihood of developing a vein occlusion. Poppers use has previously been reported to cause hepatic veno-occlusive disease, with progressive inflammation of vessels as a proposed, alternate etiology.[6]

Multiple reports indicate that poppers use among young adults is high, especially among homosexual men. In 2009, a 6-year-long Australian study reported that approximately 60% of male homosexuals in Sydney had used poppers.[7] A 2012 report from Britain found that 10% of the general population (age 16–59 years) had tried poppers.[8] Rates of poppers use may be underestimated because of patients' reluctance to disclose their use. The physiologic effects of this recreational drug can vary among individuals depending on weight, concurrent use of other medications or alcohol, depth of inhalation, and degree of physical activity undertaken before or after ingestion.

Physicians should maintain a high index of suspicion for poppers use when young patients present with a vein occlusion, particularly in homosexual patients whose laboratory tests fail to identify any hypercoagulable etiology. Such patients should be asked about the use of poppers and advised to cease their use if they are suspected in playing a contributing role.

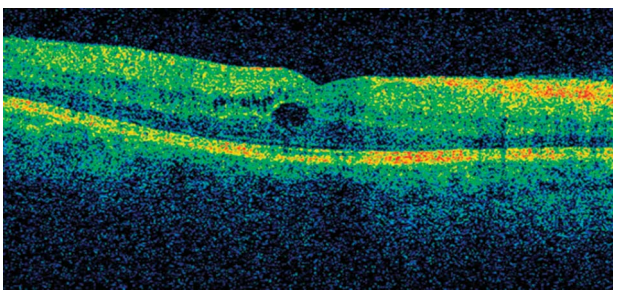

Fig. 3. Optical coherence tomography of the right macula at initial presentation demonstrating mild intraretinal edema, which resolved after intravitreal injection of bevacizumab.

Key words: alkyl nitrite, amyl nitrite, central retinal vein occlusion, poppers.

References

1. FDA Advises Consumers Not to Purchase or Use Nitrite "Poppers". U.S. Food and Drug Administration, 2021. Available at: https://www.fda.gov/food/alerts-advisories-safety-information/fda-advises-consumers-not-purchase-or-use-nitrite-poppers. Accessed January 15, 2022.
2. Hui M, Galvin J, Chilov M, et al. Popper maculopathy: long-term follow-up and case series. Retin Cases Brief Rep 2020;14:195–199.
3. Pece A, Patelli F, Milani P, Pierro L. Transient visual loss after amyl Isobutyl nitrite abuse. Semin Ophthalmol 2004;19:105–106.
4. Chrysant SG, Dunn FG, De Carvalho JG, et al. Action of nitroglycerin and amyl nitrite in labile and essential hypertension: hemodynamic differences. Arch Intern Med 1977;137:1702–1705.
5. Nossaman VE, Nossaman BD, Kadowitz PJ. Nitrates and nitrites in the treatment of ischemic cardiac disease. Cardiol Rev 2010;18:190–197.
6. Mortele KJ, Van Vlierberghe H, Wiesner W, Ros PR. Hepatic veno-occlusive disease: MRI findings. Abdom Imaging 2002;27:523–526.
7. Prestage G, Jin F, Kippax S, et al. Use of illicit drugs and erectile dysfunction medications and subsequent HIV infection among gay men in Sydney, Australia. J Sex Med 2009;6:2311–2320.
8. Davies AJ, Kelly SP, Naylor SG, et al. Adverse ophthalmic reaction in poppers users: case series of "poppers maculopathy". Eye 2012;26:1479–1486.