Temporary bilateral central scotoma under scotopic conditions associated with oral semaglutide

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Introduction

Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP1-RA) that treats type 2 diabetes mellitus and can also be used as an adjunct for weight loss when combined with exercise and diet.[1,2] It works by increasing insulin release and sensitivity.

One ophthalmic side effect of semaglutide and similar GLP1-RAs is a paradoxical increase in diabetic retinopathy, possibly due to rapid blood sugar reduction.[4,5] Other reports of macular complications and blurred vision have been reported in federal reporting systems, which have various limitations.[6,7] Here we report a case of a central, bilateral visual scotoma under scotopic conditions in a board-certified ophthalmologist (JAD), that resolved quickly following medication discontinuation. To our knowledge no prior similar case has been reported.

Case Description

A 72-year-old healthy board-certified male ophthalmologist had a history of successful cataract surgery in the right eye 18 months earlier and a mild nuclear cataract on the left when he started taking oral semaglutide to help with weight loss. 17 days after starting 3.0 mg oral semaglutide (Rybelsus) daily he observed a small, round central scotoma in his right eye (Figures 1 and 2). It appeared to enlarge over three evenings of observation, ultimately turning into an irregular square shape (Figure 3). After three days a similar but smaller scotoma was detected in his left eye.

These symptoms were observed only under scotopic conditions in a bedroom dimly lit. These symptoms were observed during the night and disappeared with natural or artificial light the next morning. When closing his eyes, a bright white afterimage of the dark scotoma faded over 5 seconds. When entering a partially lit bathroom, the scotoma took on a dark brown appearance for a fraction of a second and then disappeared.

A smaller and more subtle scotoma was observed in his left eye three evenings after the right had started. That next morning, a possible association with semaglutide was suspected and the medication was discontinued. The symptoms gradually diminished over the next two evenings and were gone after that. The timing of symptoms are summarized in Table 1.

His medications included oral semaglutide 3 mg daily for 20 days, propranolol 20 mg twice a day, aspirin 81 mg daily, naproxen 220 mg and ibuprofen 400 mg as needed. The patient returned from his vacation, upon which a formal ophthalmic evaluation was performed. His uncorrected distance visual acuity measured 20/20 right eye (OD) and 20/25 left eye (OS). The anterior segment exam was normal including a well-centered intraocular lens and clear posterior capsule. Fundus examination, Humphrey visual field testing, and Macular optical coherence tomography findings can be summarized in figures 4, 5, and 6. Retinal nerve fiber layer OCTs were normal.

Figures

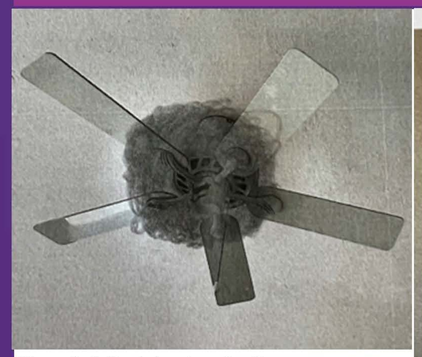

Figure 1: Patient drawing of a dim scotoma under scotopic condition covering the central portion of a ceiling fan.

Figure 2. Patient drawing of the dim scotoma projected over a portion of bedside table lamp shade. The scotoma could be projected anywhere in the room.

Figure 3. The scotoma grew over several evenings and became an irregular square-shape while the relative dimness of the scotoma remained unchanged.

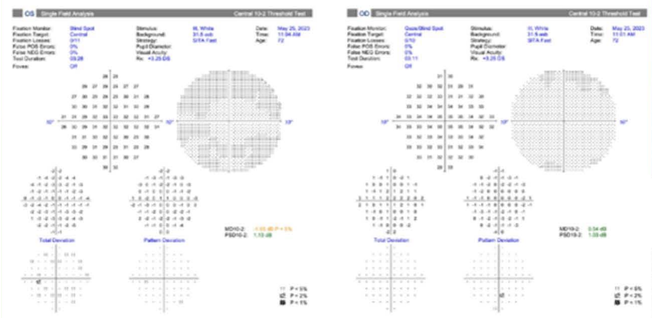

Figure 5. Humphrey visual fields reveal symmetrically normal highly reliable results for both eyes.

Figure 4. Optos fundus photography of both eyes demonstrating a mostly benign appearance with a few drusen in both eyes and a PVD in the left eye.

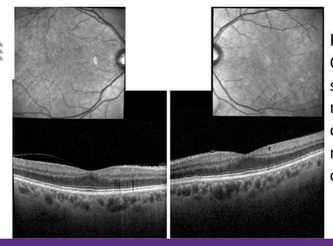

Figure 6. Macular OCTs demonstrate symmetrically minimal small drusen in with normal foveal contours.

Timeline

Date	Event
Day 0	Started 3.0 mg semaglutide in the morning
Day 16	First noticed right eye round, central scotoma
Day 17	Noticed enlarging square shape scotoma including and just below fixation
Day 19	Noticed a minimal, small and round scotoma in the left eye
Day 20	Discontinued semaglutide with 9 doses remaining (20 days total)
Day 21	Round scotoma
Day 22	Notices an enlarged scotoma covering a door panel
Day 23	Residual scotoma remaining
Day 24	Scotoma is gone

Discussion

Here we report a case of an actively practicing cataract/refractive ophthalmologist who developed a bilateral, incongruous reversible central scotoma observed only under scotopic conditions while taking semaglutide. The one known retinal side effect of semaglutide is the paradoxical worsening of diabetic retinopathy, which is not applicable here as the subject didn't have diabetes or retinopathy.

Although unknown, we postulate that the primary location of pathology in our patient may be neurosensory in nature produced by dysfunction of retinal ganglion cells. Based on the initial unilaterality of symptoms, a pre-chiasmal location of pathology might be deduced. The central, bilateral location points towards either a macular or optic nerve process.

Supporting a possible optic neuropathy cause is the distribution of GLP-1 receptors in the human retina. Some evidence localizes GLP1 receptors primarily to the retinal ganglion cells with minimal photoreceptor or RPE expression.[9] Thus, the symptoms experienced and GLP1 receptor distribution are potentially consistent and could provide a possible mechanism for the visual symptoms experienced.

Medications have shown to associate with visual phenomena, though their drug class and categorization of visual symptoms can be broad making it difficult to ascertain a specific mechanism of symptom production. Vasoactive medications and other medication-related visual side-effects can occur via progressive optic neuropathy and those with cumulative retinal toxicity such as hydroxychloroquine, known to be dose dependent and often progressive once observed.[10] These cases can have a variable level of symptomatic and functional impact for patients. Reversible, or partially-reversible, optic neuropathies can be seen with medications such as ethambutol.[11]

In conclusion, we describe a case of a bilateral, incongruous, temporary central scotoma visible only under scotopic conditions possibly due to oral semaglutide use. With the popularity of this new medication and mild symptoms, practitioners should be aware of and on the lookout for this and perhaps other possible new associations.

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