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Semaglutide-inducing Non-arteritic Anterior Ischemic Optic Neuropathy and Ipsilateral Blindness -A Rare Presentation

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Abstract

Background: Semaglutide, a glucagon-like peptide-1 receptor agonist, was approved by the FDA in 2017. It is commonly prescribed as an adjunct regimen or alternative monotherapy for patients with type 2 diabetes who have failed initial treatment with metformin and lifestyle modification. Semaglutide is well known for its benefits in blood glucose control, weight loss, and reducing the risk of major atherosclerotic cardiovascular disease (ASCVD), including stroke and heart attack. It has been increasingly prescribed in cardiology offices to control risk factors for ASCVD. A recent cohort study showed an association between semaglutide use and the development of non-arteritic anterior ischemic optic neuropathy.

Case presentation: A 63-year-old male patient presented to his cardiologist's office for a hospital follow-up after a sudden onset of right lower visual field loss due to optic nerve edema. It was a sudden onset of lower visual field loss in the right eye, progressing upward with pain over his right temporal area after taking semaglutide for one year. In the hospital, a CT head, MRI of the orbit, carotid ultrasound, echocardiogram, and temporal artery biopsy were all negative for any ischemic, embolic, or inflammatory processes. The patient's negative workup during admission suggested a possible diagnosis of exclusion: semaglutide-associated optic neuropathy.

Conclusion: This case highlights a rare but potentially serious adverse effect of semaglutide. Physicians should be aware of the possibility of iatrogenic optic edema, sudden vision loss, and early signs of such side effects secondary to semaglutide use. Education should be provided to every patient taking semaglutide.

Keywords: Semaglutide, Non-arteritic anterior ischemic optic neuropathy, Vison loss, Cardiovascular Risk Reduction, Cardiovascular Therapeutics

Introduction

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common cause of optic nerve edema and neuropathy, involving the axons that make up the optic nerve but not including the optic nerve head (also known as posterior ischemic optic neuropathy). Anterior ischemic optic neuropathy can be further divided into arteritic (giant cell arteritis) and non-arteritic subtypes [1]. The pathophysiology of NAION remains unclear and is currently thought to result from impaired blood flow in the posterior ciliary arteries that supply these segments of the optic nerve [2]. The use of glucagon-like peptide-1 (GLP-1) receptor agonists, such as semaglutide, has risen significantly in cardiology clinics, where they are utilized for managing diabetes and weight to better control ASCVD risk factors. A growing number of cases are being studied that suggest a potential association between semaglutide and adverse ocular events such as NAION [3]. This case report presents a potentially serious complication of semaglutide associated with vision loss.

We report a case of a patient taking semaglutide who developed permanent vision loss after exclusion of other possible diagnosis.

The information contained in this clinical case description was obtained through a review of medical records, patient reports, images of diagnostic tests, and literature review.

Case Presentation

A 63-year-old male patient with a past medical history of essential hypertension, hyperlipidemia, type 2 diabetes, hypothyroidism, and sleep apnea presented to the cardiology office for a follow-up after being hospitalized for non-arteritic anterior ischemic optic neuropathy, which was preceded by the sudden onset of right optic edema, lower half vision loss, and right temporal pain.

The patient was initially prescribed semaglutide 0.25 mg as a weekly subcutaneous injection one year ago for weight loss and type 2 diabetes control in the cardiology office. HbA1C was 7.0% and BMI was 35. The patient responded well to the therapy, with HbA1C improving to 5.7% and BMI reducing to 28 after 4 months of treatment. The dosage was increased to 0.5 mg at the patient's request for further weight control. No history of diabetes complications was noted, including diabetic retinopathy, gastroparesis, albuminuria, neuropathy, or foot ulcers. Current medications include aspirin, atorvastatin, fluoxetine, levothyroxine, lisinopril, metformin, metoprolol succinate, montelukast, semaglutide, and icosapent ethyl.

The patient initially noticed crust formation on the right lower eyelid, accompanied by 20% blurriness in the lower visual field, 10 days before hospitalization. He described it as complete blackness in the lower visual field with blurriness along the upper edge. Vision loss gradually progressed to 50%, prompting the patient to visit his ophthalmologist. The patient's right eye vision was 20/25, and he was found to have right superior sectoral optic nerve edema with an inferior hemifield defect. He was immediately referred to the emergency room for hospitalization and further ischemic workup. Upon hospitalization, initial physical examination was negative for any focal neurological deficits or signs of stroke. Fundoscopy revealed right optic edema. Over a 2-day hospital stay, imaging and laboratory workup included a CT head scan, MRI of the orbit with and without contrast, carotid duplex ultrasound, echocardiogram, right temporal artery biopsy, and inflammatory markers. Results were negative for ischemic, thromboembolic, or inflammatory processes. The patient was presumably diagnosed with idiopathic optic neuropathy. At the ophthalmology follow-up visit after discharge, the patient's right vision was 20/100 with changes to the blind spot. He was prescribed prednisolone acetate eye drops to control the progression of optic edema and vision loss. A diagnosis of NAION with abnormal cupping was officially made. Two weeks later, despite using prednisolone eye drops, the patient's vision loss worsened, progressing to 80% loss of the inferior visual field with cloudiness in the remaining 20%. His right eye vision worsened to counting fingers at 3 feet (CF3ft), with further changes to the blind spot. He was prescribed oral prednisone 60 mg daily, which eventually stopped the progression of vision loss. The patient stopped the medication 2 months after stabilization of vision loss. He was declared legally blind in the right eye.

Discussion

The differential diagnosis for this patient included acute-on-chronic diabetic retinopathy, nocturnal hypoperfusion secondary to antihypertensive medications, giant cell arteritis, carotid artery stenosis, and idiopathic optic neuropathy.

In the hospital, a transthoracic echocardiogram (TTE) showed that the ejection fraction was 60-65%. All four chambers were normal in size without abnormal wall motion or thickness except for mild sclerosis in aortic valve. MRI orbit with and without contrast showed unremarkable appearance of the orbits. No signs of abnormality or mass were found in the ocular globes, extraocular muscles, optic nerve sheath, or lacrimal glands. The optic nerves, optic chiasm, and optic tracts were within normal limits. No signal abnormality, mass, or abnormal enhancement were found in cavernous sinuses, basal cisterns, or brain parenchyma. The sensitivity and specificity of MRI orbit for NAION were uncertain. However, MRI orbit was typically normal without any signs of abnormality in patients with NAION [4]. The presence of enhancement in optic nerve, optic chiasm, or optic tracts indicates inflammatory process or other etiologies.

Electrocardiograms (EKG) from the cardiology office, one before and one after the onset of vision loss, showed normal sinus rhythm without findings suggesting arrhythmia or ischemia. A 2-week recording from a Holter monitor after vision loss showed predominantly normal sinus rhythm with less than 0.1% of premature atrial contraction (PAC) or premature ventricular contraction (PVC). No atrial fibrillation or atrial flutter was recorded, ruling out possible embolic cause of the vision loss.

NAION is an irreversible disease. The most common presenting symptom is monocular loss of vision occurring over hours to days. Symptoms may be present upon awakening, as observed in this patient [5]. Altitudinal vision loss has been reported in some cases, including this one [5]. After the onset of symptoms, vision may continue to deteriorate over the first few days or weeks. After the initial period of visual decline, most patients stabilize, and the progression of vision loss stops. Recovery of visual fields is uncommon, and most patients do not experience significant improvement in their vision, resulting in permanent vision loss [6].

The treatment of NAION remains a topic of debate. No effective medical therapy has been proven to alleviate or restore visual function [7]. Aspirin and glucocorticoids have

been studied in the past, but neither has shown any benefit in slowing or reversing vision impairment. A previous study found that aspirin therapy does not influence the visual outcomes of acute NAION [8]. Similarly, glucocorticoids are not recommended for treating NAION due to limited evidence supporting their efficacy and benefit. However, glucocorticoids are sometimes used in NAION when there is concern that giant cell arteritis has not been ruled out, as observed in this case [9]. Surgical therapies, such as optic nerve sheath decompression and optic neurotomy, may be considered in select cases. However, there is limited evidence to support the benefits of these procedures. Therefore, in most cases, the treatment of NAION primarily focuses on supportive care, including assistance with daily activities and transportation, social and psychological support, and the prevention of further complications.

Previous studies have shown a higher incidence of ophthalmologic complications associated with diabetes and obesity [10]. These complications were mainly observed in patients with preexisting diabetic retinopathy who experienced a rapid reduction in HbA1c during the first 16 weeks of treatment [11]. However, the patient in this case had no history of diabetic retinopathy. The total reduction of 1.3% in HbA1c, combined with the onset of vision loss after 16 weeks, makes rapid correction of HbA1c an unlikely cause of the pathogenesis. The ophthalmologist evaluating the patient considered nocturnal hypoperfusion due to antihypertensive medications. However, this was less likely since the patient was taking metoprolol succinate at bedtime, a long-acting beta-blocker that does not peak within 4–6 hours of sleep.

A recent observational study has suggested a potential association between NAION and semaglutide [3]. The study showed that among individuals with type 2 diabetes, the cumulative incidence of NAION was 8.9% for semaglutide users compared to 1.8% for non-semaglutide users. Similarly, among individuals with obesity, the cumulative incidence was 6.7% for semaglutide users compared to 0.8% for non-semaglutide users, findings that were both statistically and clinically significant [3]. The pathogenesis of NAION in semaglutide users is not fully understood; however, the incidence of NAION has been reported to range from 2 to 10 cases per 100,000, making it the second most common cause of blindness due to optic nerve damage [3].

The Adverse Drug Reaction Probability Scale (Naranjo Algorithm) score is a method for estimating the probability of adverse drug reactions [12]. In this case, the Naranjo Algorithm for semaglutide causing NAION is 3, categorizing it as 'possible,' meaning that semaglutide could independently contribute to the development of NAION. A previous cohort study reported a positive association between semaglutide and NAION (+1 score) [3]. The adverse event occurred after semaglutide administration (+2 score). The progression of vision loss ceased after semaglutide was discontinued (+1 score). Finally, alternative causes that could independently lead to the development of NAION were identified (-1 score).

This patient had both type 2 diabetes and obesity at the start of treatment, placing him at a higher baseline risk of developing NAION compared to those with type 2 diabetes alone (1.8% baseline risk) [3], obesity alone (0.8% baseline risk) [3], or neither condition (2–10 per 100,000 baseline risk) [3]. His medical history also includes obstructive sleep apnea, hypertension, and hypercholesterolemia, all of which are significant risk factors for developing NAION [13]. Given his chronic medical conditions, long-term use of semaglutide, and negative ischemic workup results, a diagnosis of NAION secondary to semaglutide use is suggested by excluding other potential causes. He may develop NAION in the future even without taking semaglutide, given his high baseline risk due to multiple factors. However, his use of semaglutide increases the likelihood of NAION and accelerates its progression.

Conclusion

This case emphasizes the importance of early recognition of this adverse effect to prevent long-term or permanent vision loss in patients treated with semaglutide for diabetes and weight management. Physicians should be aware of possible iatrogenic optic edema, sudden vision loss, and the early signs of such side effects associated with semaglutide use.

Recommendation

Further investigation is needed to explore this medication's association with newly onset vision loss. Educating patients on early recognition of such symptoms when prescribing semaglutide may reduce the number of cases of permanent vision loss. If any of these symptoms occur, patients should discontinue the medication immediately and seek medical advice.

Disclaimer

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