JOURNAL OF DIABESITY | ADVANCING METABOLIC HEALTH | ISSN: PENDING

Suspected Optic Nerve Dysfunction Associated with Semaglutide in a Non-Diabetic Obese Patient: A Case Report

Authors:

Badeeya Rashid[*1], Fareha Rasheed[1], Sibghatullah[1]

[1] Department of General Medicine, Pakistan Institute of Medical Sciences, Islamabad Capital Territory, Islamabad, Pakistan.

*Corresponding Author: badeeyaj@gmail.com

Rashid B, Rasheed F, Sibghatullah, Wains AA. *Suspected optic nerve dysfunction associated with semaglutide in a non-diabetic obese patient: a case report. J Diabesity. 2026;1(2). Available from: https://journalofdiabesity.com/ojs-files/index.php/diabesity/article/view/8*

Abstract:

Background: Semaglutide, a glucagon-like peptide-1 receptor agonist, is widely used for the treatment of type 2 diabetes mellitus and obesity. Although its safety profile is well established for common adverse effects, reports of neuro-ophthalmic complications remain limited.

Case Presentation: A middle-aged non-diabetic obese man with a history of non-specific vasculitis and chronic lymphedema developed persistent bilateral blurred vision after initiation of semaglutide for weight management. He had no prior history of hypertension, dyslipidemia, or ocular disease. Comprehensive ophthalmologic examination was normal. Despite discontinuation of semaglutide, visual symptoms persisted. Neurologic evaluation raised concern for optic nerve involvement, although neuroimaging was inconclusive.

Outcome: The temporal association with semaglutide exposure and the absence of alternative causes suggested a possible drug-associated neuro-ophthalmic adverse effect. The patient experienced psychological distress related to persistent visual impairment and weight regain.

Conclusion: This case highlights a potential association between semaglutide therapy and optic nerve–related visual disturbance in a non-diabetic patient. Clinicians should consider neuro-ophthalmic evaluation in patients receiving GLP-1 receptor agonists who develop new visual symptoms.

Rashid B, Rasheed F, Sibghatullah, Wains AA. *Suspected optic nerve dysfunction associated with semaglutide in a non-diabetic obese patient: a case report. J Diabesity. 2026;1(2). Available from: https://journalofdiabesity.com/ojs-files/index.php/diabesity/article/view/8*

Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are widely used for the treatment of type 2 diabetes mellitus and obesity, owing to their demonstrated efficacy in improving glycemic control and inducing clinically meaningful weight loss. Semaglutide, a long-acting GLP-1 RA, has been adopted across a broad range of clinical settings and is increasingly prescribed for weight management in both diabetic and non-diabetic populations.

The safety profile of semaglutide is well characterized with respect to common gastrointestinal and metabolic adverse effects. However, with expanding use in real-world practice and the evaluation of higher-dose regimens (up to 7.2 mg per week), uncommon and potentially serious adverse events may be increasingly recognized[1]. Although higher doses have been associated with greater weight reduction, they have also been linked to a higher frequency of adverse effects, underscoring the importance of careful attention to emerging dose-related safety signals, including rare neuro-ophthalmic complications such as optic neuropathy and optic neuritis.

The mechanisms by which GLP-1 RAs might contribute to optic nerve dysfunction are not well defined[2]. Proposed hypotheses include alterations in optic nerve perfusion, microvascular regulation, immune-mediated inflammatory effects, and indirect consequences of rapid metabolic or weight changes. These mechanisms

may be particularly relevant in patients with underlying inflammatory or vascular conditions, although supporting evidence remains sparse.

Given the expanding use of semaglutide for obesity in individuals without traditional cardiometabolic comorbidities, recognition of rare neuro-ophthalmic adverse events is of increasing clinical importance[3]. Early identification of drug-associated visual symptoms is critical, as optic nerve pathology may lead to persistent or irreversible visual impairment.

Here, we report a case of persistent bilateral blurred vision with suspected optic nerve involvement temporally associated with semaglutide therapy in a non-diabetic obese patient, despite normal ophthalmologic examination. This case highlights the need for heightened clinical awareness and further investigation into potential neuro-ophthalmic effects of GLP-1 receptor agonists.

Case Presentation

A middle-aged man with a history of non-specific vasculitis, chronic lymphedema, and obesity (body mass index, 42.61 kg/m^2) was started on semaglutide for pharmacologic weight management. He had no history of diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, or known ocular or neurologic disorders. There was no family history of optic neuropathy, demyelinating disease, or other neuro-ophthalmic conditions. He was not receiving medications known to be associated with optic nerve toxicity.

Semaglutide was initiated at a standard starting dose of 0.25 mg weekly and titrated to 1 mg subcutaneous weekly, according to recommended protocols. Several weeks after treatment initiation, the patient reported the onset of persistent bilateral blurred vision. The visual symptoms were continuous and non-fluctuating. He denied eye pain, pain with eye movement, photophobia, diplopia, headache, nausea, vomiting, focal weakness, sensory symptoms, or other neurologic complaints.

Comprehensive ophthalmologic evaluation showed best-corrected visual acuity within age-appropriate limits. Slit-lamp examination revealed no anterior segment abnormalities. Intraocular pressure was within the normal range in both eyes. Dilated funduscopic examination demonstrated normal-appearing optic discs without edema, pallor, or hemorrhage. The macula and peripheral retina were unremarkable, with no evidence of retinopathy, vasculitic changes, or other retinal pathology. Repeat ophthalmologic examination at follow-up similarly revealed no structural abnormalities.

Given the temporal association between symptom onset and initiation of semaglutide, the medication was discontinued. Despite discontinuation, the patient reported persistence of blurred vision with minimal subjective improvement during follow-up. Owing to ongoing symptoms and normal ophthalmologic findings, neurologic consultation was obtained. Clinical evaluation raised concern for possible optic nerve involvement, including optic neuritis; however, neuroimaging

did not demonstrate definitive evidence of demyelination, compressive lesions, or other structural abnormalities.

Laboratory testing, including inflammatory markers and autoimmune studies (ANA and ANCA Profile) where obtained, did not identify an alternative systemic cause. There was no evidence of acute infection, metabolic disturbance, or toxic exposure. The absence of conventional vascular risk factors and the lack of diagnostic findings limited identification of an alternative explanation for the visual disturbance.

The persistent visual symptoms were associated with substantial psychological distress. The patient reported anxiety and low mood related to ongoing visual impairment and discontinuation of semaglutide, which was followed by partial weight regain. He was referred for psychiatric evaluation and supportive management.

Overall, the close temporal relationship between semaglutide initiation and the onset of bilateral blurred vision, combined with the absence of pre-existing ocular disease, conventional vascular risk factors, or alternative diagnostic findings, raised concern for a possible drug-associated neuro-ophthalmic adverse effect.

Discussion:

This case describes persistent bilateral visual disturbance with suspected optic nerve involvement temporally associated with initiation of semaglutide therapy in

a non-diabetic obese patient. The close temporal relationship, absence of alternative identifiable causes, and persistence of symptoms after drug discontinuation support a possible association between semaglutide exposure and optic nerve dysfunction. Although causality cannot be established on the basis of a single case, the findings are consistent with emerging concerns regarding rare neuro-ophthalmic adverse events associated with glucagon-like peptide-1 receptor agonists (GLP-1 RAs)[3].

Semaglutide has demonstrated substantial efficacy in glycemic control and weight reduction and is widely prescribed in both diabetic and non-diabetic populations[4, 5]. In large randomized clinical trials, the most commonly reported adverse events have been gastrointestinal, and serious neuro-ophthalmic complications have been reported infrequently. However, clinical trials are not designed to reliably detect rare adverse events. Post-marketing surveillance and case-based reports have increasingly identified visual disturbances temporally associated with GLP-1 RA therapy, including reports of non-arteritic anterior ischemic optic neuropathy and optic neuritis[6]. These observations suggest that uncommon optic nerve–related adverse effects may be underrecognized.

Several mechanisms may plausibly link GLP-1 RA therapy to optic nerve dysfunction. Alterations in systemic hemodynamics and microvascular regulation could affect optic nerve head perfusion, particularly in susceptible individuals. Even modest changes in perfusion pressure may be clinically relevant for the optic nerve, which is sensitive to ischemic and inflammatory injury. In addition, GLP-1

receptors are expressed in central nervous system tissues, raising the possibility of direct or indirect effects on neuroinflammatory pathways[7].

In this patient, the presence of underlying non-specific vasculitis may represent a potential susceptibility factor. Immune-mediated mechanisms or microvascular inflammation could theoretically lower the threshold for optic nerve injury in the setting of additional physiological stressors. Although neuroimaging did not demonstrate definitive inflammatory changes, subclinical or transient optic nerve inflammation cannot be excluded. Early or retrobulbar optic neuritis may present with initially normal funduscopic findings, and neuroimaging may be insensitive in atypical or early presentations[8].

Rapid metabolic and weight changes associated with semaglutide therapy may also contribute indirectly to optic nerve vulnerability[9]. Alterations in neurovascular regulation or intracranial pressure dynamics have been proposed in other clinical contexts, although direct evidence linking these mechanisms to GLP-1 RA–associated optic neuropathy is limited. Distinguishing direct drug effects from secondary physiological consequences of substantial weight loss remains challenging.

The absence of conventional vascular risk factors, including diabetes mellitus, hypertension, and dyslipidemia, strengthens the significance of this observation. Normal ophthalmologic examinations and inconclusive neuroimaging limited

diagnostic certainty but do not exclude clinically meaningful optic nerve dysfunction. The bilateral nature of symptoms and persistence after drug withdrawal further support consideration of a systemic or medication-related mechanism.

Beyond the visual symptoms, this case illustrates the broader clinical impact of suspected adverse drug reactions. The patient experienced psychological distress related to persistent visual impairment and discontinuation of effective weight-loss therapy, with subsequent weight regain and depressive symptoms[10]. These consequences highlight the importance of considering both physical and psychosocial outcomes when evaluating and managing potential adverse effects of obesity pharmacotherapy.

This report has important limitations. As a single case, it cannot establish causality, and unrecognized confounding factors cannot be excluded. Objective confirmation of optic neuritis or a specific optic neuropathy subtype was not obtained. Dose–response relationships, rechallenge data, and systematic pharmacovigilance analyses are lacking. Nonetheless, the temporal association, exclusion of common alternative etiologies, and consistency with emerging post-marketing signals support the plausibility of a drug-associated effect.

From a clinical perspective, this case underscores the importance of vigilance for neuro-ophthalmic symptoms in patients receiving GLP-1 receptor agonists,

including those without traditional vascular or ocular risk factors. New-onset visual symptoms should prompt timely multidisciplinary evaluation and consideration of medication-related causes. In selected patients with inflammatory or vascular comorbidities, a lower threshold for neuro-ophthalmic assessment may be appropriate.

In summary, this case supports growing evidence that semaglutide and other GLP-1 receptor agonists may, in rare instances, be associated with optic nerve–related visual disturbances. While these agents remain highly effective and generally safe, recognition of uncommon but potentially serious neuro-ophthalmic adverse effects is important. Larger observational studies, systematic pharmacovigilance efforts, and mechanistic investigations are needed to better define risk, clarify causality, and inform evidence-based monitoring strategies.

Conclusion:

This case suggests a possible association between semaglutide therapy and persistent visual disturbance with suspected optic nerve involvement. Clinicians should consider neuro-ophthalmic evaluation for new visual symptoms in patients receiving GLP-1 receptor agonists.

Consent:

Written informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest:

The authors declare no conflicts of interest.

Funding:

No funding was received for this study.

References:

1. Wharton S, Freitas P, Hjelmesæth J, Kabisch M, Kandler K, Lingvay I, Quiroga M, Rosenstock J, Garvey WT. Once-weekly semaglutide 7· 2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial. The Lancet Diabetes & Endocrinology. 2025 Nov 1;13(11):949-63.

2. Wang L, Volkow ND, Kaelber DC, Xu R. Semaglutide or tirzepatide and optic nerve and visual pathway disorders in type 2 diabetes. JAMA Network Open. 2025 Aug 11;8(8):e2526327.

3. Cai CX, Hribar M, Baxter S, Goetz K, Swaminathan SS, Flowers A, Brown EN, Toy B, Xu B, Chen J, Chen A. Semaglutide and nonarteritic anterior ischemic optic neuropathy. JAMA ophthalmology. 2025 Apr;143(4):304-14.

4. Chen B, Tao L, Tian M, Ji Z. Efficacy and safety of combination of semaglutide and basal insulin in patients with of type 2 diabetes mellitus: A systematic review and meta-analysis. Clinical Nutrition ESPEN. 2025 Jan 30.

5. Salvador R, Moutinho CG, Sousa C, Vinha AF, Carvalho M, Matos C. Semaglutide as a GLP-1 agonist: A breakthrough in obesity treatment. Pharmaceuticals. 2025 Mar 12;18(3):399.

6. Feng JN, Chen Y, Jin T. GLP-1 medicine and nonarteritic anterior ischemic optic neuropathy: literature review and perspectives. Metabolism and Diseases. 2025 Dec 8:100001.

7. West J, Li M, Wong S, Le GH, Teopiz KM, Valentino K, Dri CE, McIntyre RS. Are Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists Central

Nervous System (CNS) Penetrant: A Narrative Review. Neurology and therapy. 2025 Apr 2:1-0.

8. Eggenberger E. Optic neuritis. CONTINUUM: Lifelong Learning in Neurology. 2025 Apr 1;31(2):407-35.
9. Gong X, Örge FH. Glucagon-like Peptide-1 Receptor Agonists and Ocular Disease: Mechanisms, Evidence and Therapeutic Perspectives.
10. West S, Scragg J, Aveyard P, Oke JL, Willis L, Haffner SJ, Knight H, Wang D, Morrow S, Heath L, Jebb SA. Weight regain after cessation of medication for weight management: systematic review and meta-analysis. bmj. 2026 Jan 7;392.