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Obsessive-Compulsive Symptoms after Tirzepatide Treatment: A Case Report

Gözde Özsoy Şen[1], Rıdvan Sivritepe[2*], Sema Basat Uçak[1]

1. Department of Internal Medicine, Umraniye Education and Research Hospital, University of Health Sciences, 34764 Ümraniye, İstanbul, Türkiye.

2. Department of Internal Medicine, Faculty of Medicine, Istanbul Medipol University, 34893 Pendik, İstanbul, Türkiye.

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ABSTRACT

Obsessive-compulsive disorder (OCD) is a chronic psychiatric disorder characterized by obsessions and compulsions that are time-consuming, distressing, and cause significant impairment in functioning. Obsessions are recurrent, intrusive, and unwanted thoughts, urges, or images, while compulsions are repetitive behaviors or mental acts performed to reduce the distress associated with these obsessions or to prevent perceived harm. OCD affects approximately 1–3% of the population and typically begins in adolescence or early adulthood. If left untreated, it usually follows a chronic or progressive course.

A 29-year-old male with a two-year history of obesity presented to our clinic for weight management. His body mass index (BMI) was calculated as 36.1 kg/m². The patient had previously been treated with metformin for insulin resistance; however, therapy was discontinued after three months because of gastrointestinal intolerance, and tirzepatide was then initiated. At the 11th dose of tirzepatide, the patient reported a three-week history of worsening intrusive thoughts and increased stress, for which he was referred to psychiatry. His family history revealed that his father had been diagnosed with OCD for 20 years. The patient was diagnosed with OCD by the psychiatry department and initiated on psychotherapy and a selective serotonin reuptake inhibitor (SSRI), with subsequent improvement of his obsessions and compulsions.

Introduction

OCD is a chronic psychiatric condition characterized by obsessions and compulsions that are time-consuming, distressing, and cause significant functional impairment. Obsessions are recurrent, intrusive, and unwanted thoughts, urges, or images, while compulsions are repetitive behaviors or mental acts performed to reduce distress or prevent potential harm. OCD affects 1–3% of the population and typically begins in adolescence or early adulthood [1]. The etiology of OCD is multifactorial, involving cognitive, genetic, molecular, environmental, and neurobiological factors [2].

The diagnosis of OCD is based on clinical evaluation and the criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR).* These criteria require the

*** Corresponding Author:**
Rıdvan Sivritepe MD
Address: *Bahcelievler Quarter, Adnan Menderes Boulevard No:31 Pendik Istanbul, Türkiye.*
E-mail: *ridvan.sivritepe@medipol.edu.tr*

presence of obsessions and compulsions that are time-consuming (occupying more than one hour per day) and cause significant impairment in daily life [3].

Tirzepatide is a single molecule that combines glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonism [4]. It has been approved for the treatment of type 2 diabetes mellitus (T2DM) and obesity. With the global rise in obesity, tirzepatide has emerged as a promising non-surgical treatment option. The most frequently reported adverse effects include nausea, vomiting, dyspeptic symptoms, and myalgia. Reported psychiatric side effects have mainly involved depression and increased suicidal ideation. To our knowledge, this is the first reported case of new-onset obsessive–compulsive disorder associated with tirzepatide use, suggesting a potential neuropsychiatric link warranting further investigation [5].

Compared to other injectable anti-obesity treatments, tirzepatide is associated with fewer neuropsychiatric adverse effects. Pharmacovigilance analysis of the Food and Drug Administration Adverse Event Reporting System (FAERS) between 2004 and 2024 revealed significant safety signals of depression and suicidal ideation with semaglutide when used for weight management, whereas tirzepatide appeared to have a more favorable psychiatric safety profile [6]. Herein, we report a unique case of new-onset obsessive–compulsive disorder temporally associated with tirzepatide treatment for obesity.

Case Presentation

A 29-year-old male with a two-year history of obesity presented to our clinic for weight management. On physical examination, his general condition was good, and he was conscious. Head and neck examination revealed no abnormalities. There was no scleral icterus, conjunctivae appeared normal, and no lymphadenopathy was detected. The thyroid gland was non-palpable and non-nodular. There was no pretibial edema. Chest auscultation was unremarkable, and costophrenic angles were clear. Cardiovascular examination showed regular S1 and S2 heart sounds without additional pathological findings. Abdominal examination revealed three non-violaceous striae in the lower abdomen. Neurological examination was normal.

Vital signs were within normal limits: arterial blood pressure 125/78 mmHg, pulse 82 bpm, and body temperature 36.2 °C. Electrocardiography demonstrated normal sinus rhythm without ischemic changes. He had a history of dietary intervention for obesity at the age of 20. At the age of 24, he was treated with metformin 1000 mg twice daily for six months due to insulin resistance. During that period, he lost 3 kilograms (kg) with exercise and metformin therapy. Family history was notable for OCD in his father and generalized anxiety disorder in his sibling. He was an ex-smoker with a 3 pack-year history.

His height and weight were measured, and his body mass index (BMI) was calculated as 36.1 kg/m². Serum blood samples were collected. The patient's liver and kidney function tests, as well as glucose, insulin, and uric acid levels, were within normal ranges (Table 1). In the endocrine evaluation, morning serum cortisol and ACTH levels were within the normal reference range. As the patient exhibited no clinical features suggestive of Cushing syndrome and the initial hormonal profile was normal, further dynamic testing (including the 1-mg overnight dexamethasone suppression test and 24-hour urinary free cortisol measurement) was not deemed necessary.

Tirzepatide was initiated for obesity management. He received 2.5 mg subcutaneously once weekly for

Table 1. Laboratory parameters at baseline

Parameter	Result	Reference Range
Fasting Glucose	78 mg/dL	74 – 106 mg/dL
Insulin	12.3 mU/L	2.6 – 24.9 mU/L
HOMA-IR	2.37	< 2.5
LDL-Cholesterol	105 mg/dL	0 – 130 mg/dL
HDL-Cholesterol	47 mg/dL	35 – 55 mg/dL
Total Cholesterol	170 mg/dL	0 – 200 mg/dL
Triglycerides	88 mg/dL	0 – 150 mg/dL
Blood Urea Nitrogen	18 mg/dL	7 – 20 mg/dL
Creatinine	1.28 mg/dL	0.7 – 1.2 mg/dL
Uric Acid	8.14 mg/dL	3.4 – 7.0 mg/dL
Aspartate Aminotransferase	18 U/L	0 – 40 U/L
Alanine Aminotransferase	19 U/L	0 – 41 U/L
Adrenocorticotropic Hormone	13.28 ng/L	7.2 – 63.3 ng/L
Cortisol	11.9 ng/L	4.82 – 19.5 ng/L

Table 2. Naranjo Adverse Drug Reaction Probability Scale.

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1			+1
2. Did the adverse event appear after the suspected drug was administered?	+2			+2
3. Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered?	+1			+1
4. Did the adverse reaction reappear when the drug was re-administered?		0		0
5. Are there alternative causes that could have caused the reaction?		-1		-1
6. Did the reaction reappear when a placebo was given?			0	0
7. Was the drug detected in any body fluid in toxic concentrations?			0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1			+1
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?		0		0
10. Was the adverse event confirmed by any objective evidence?	+2			+2
Total Score				6 (Probable)

Table 3. Change in Yale–Brown Obsessive–Compulsive scale scores before and after treatment.

Y-BOCS Item	Baseline Score	After Treatment Score
1. Time occupied by obsessive thoughts	3	1
2. Interference due to obsessive thoughts	3	1
3. Distress associated with obsessive thoughts	3	1
4. Resistance against obsessions	2	1
5. Degree of control over obsessive thoughts	3	1
6. Time spent performing compulsive behaviors	3	2
7. Interference due to compulsions	3	2
8. Distress if compulsions are prevented	3	1
9. Resistance against compulsions	2	0
10. Degree of control over compulsions	3	1
Total Score	28 (Severe)	11 (Mild)

Timeline: Tirzepatide initiated (week 0) → dose escalation to 5 mg (week 5) → onset of OCD symptoms (week 8) → psychiatric referral (week 11).

4 weeks, followed by 5 mg once weekly for 7 weeks. After the 8th week of tirzepatide treatment, he developed increased frequency of handwashing and intrusive fears that something bad might happen. Due to worsening symptoms, he was referred to the psychiatry department, where he was diagnosed with OCD according to DSM-5-TR criteria. During the psychiatric evaluation, the patient was assessed and examined for major depressive disorder, generalized anxiety disorder, and substance use disorder; these conditions were ruled out. Psychotherapy was initiated, and pharmacological treatment with fluoxetine 20 mg daily was prescribed.

According to the Naranjo Adverse Drug Reaction Probability Scale, the total score was calculated as 6, indicating a probable level of causality (Table 2).

At baseline, the total score on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was 28 (severe level). Following SSRI therapy and cognitive-behavioral therapy, the score decreased to 11 (mild level) (Table 3).

Discussion

OCD is characterized by the presence of obsessions and compulsions. Obsessions are intrusive, repetitive, and persistent thoughts, urges, or images, often associated with anxiety, whereas compulsions are repetitive behaviors or mental acts performed in response to obsessions, either according to rigid rules or to achieve a sense of completeness [3].

While children may have difficulty identifying obsessions, most adults recognize both their obsessions and compulsions, often acknowledging their excessiveness but feeling unable to control them [3]. The etiology of OCD is complex, involving cognitive, genetic, molecular, environmental, and neurobiological contributors [2].

Obesity is a serious, chronic, progressive, and relapsing disease. Lifestyle interventions remain the cornerstone of obesity treatment; however, sustaining weight loss achieved through caloric restriction is often challenging. Therefore, current

guidelines recommend the adjunctive use of anti-obesity medications to facilitate weight reduction, support weight maintenance, and improve health outcomes [7].

Tirzepatide combines GIP and GLP-1 receptor agonism into a single molecule, exerting synergistic effects on appetite regulation, food intake, and metabolic function. It has been approved for T2DM in the United States, European Union, and Japan, and for obesity in the United States and the United Kingdom, as a once-weekly subcutaneous injection [8].

Native GLP-1 is secreted by preproglucagon neurons in the central nervous system (CNS) [2]. In patients with obesity and T2DM, the blood–brain barrier may be altered or impaired. Tirzepatide is believed to cross the CNS slowly, likely through paracellular pathways. GLP-1 receptor agonists act directly or indirectly on CNS GLP-1 receptors, reducing energy intake, enhancing satiety, facilitating insulin signaling, and mediating other central effects [9].

The most commonly reported adverse events of tirzepatide include nausea, vomiting, abdominal pain, dyspepsia, decreased appetite, cholelithiasis, and pancreatitis. Pharmacovigilance analysis of FAERS data between 2004 and 2024 indicated significant signals of depression and suicidal ideation with semaglutide for weight management, whereas tirzepatide demonstrated a comparatively safer psychiatric profile [6].

In our case, the patient had a prior history of impulsive eating behavior and alcohol consumption. Following tirzepatide initiation, appetite suppression and discontinuation of alcohol use (due to potential interactions with tirzepatide) coincided with the emergence of obsessive symptoms. With a positive family history of OCD, the patient was subsequently diagnosed and treated by psychiatry.

The Naranjo Adverse Drug Reaction Probability Scale score was 6, indicating a probable relationship between tirzepatide use and the emergence of obsessive–compulsive symptoms. However, the fact that the drug was not discontinued represents a limitation in terms of dechallenge. The improvement of symptoms with SSRI therapy and psychotherapy complicates the causal interpretation. Nevertheless, the temporal relationship, the worsening of symptoms with dose escalation, and the exclusion of alternative causes suggest that this case is noteworthy from a pharmacovigilance perspective.

In addition, according to the DSM-5 criteria, the patient was diagnosed with obsessive–compulsive disorder (OCD), while comorbid conditions such as depression, anxiety, and substance use disorders were ruled out through detailed clinical evaluation. Considering the heterogeneity of psychiatric disorders, it is important to carefully assess possible comorbidities during the diagnostic process. Moreover, the reduction in symptom severity was objectively documented by the decrease in the Yale–Brown Obsessive Compulsive Scale (Y-BOCS) score from 28 to 11, indicating a marked clinical improvement and supporting that the obsessive–compulsive symptoms emerging after tirzepatide treatment responded to therapy.

Neuropsychiatric findings such as depressive symptoms, anxiety, and even suicidal ideation have been reported in the literature in association with GLP-1 receptor agonists. However, some studies have also suggested that these agents might exert antidepressant effects. Camkurt et al. reported that liraglutide may have neuroprotective and cognitive benefits, and that large phase 2 and 3 trials have generally found it to be safe from a neuropsychiatric standpoint. These findings suggest that GLP-1 receptor agonists may influence central nervous system functions through multiple mechanisms. While previous case reports have described depression or anxiety related to these agents, this case differs in that obsessive–compulsive symptoms developed following tirzepatide use. This highlights that the mood and behavioral effects of GLP-1 receptor activation may vary among individuals and emphasizes the need for close psychiatric monitoring in patients receiving these drugs [10].

It remains debatable whether the obsessive–compulsive symptoms observed in this case represent a new adverse reaction to tirzepatide treatment or an exacerbation of a previously latent obsessive–compulsive tendency. The patient reported only social alcohol consumption; thus, neuropsychiatric effects related to alcohol withdrawal were unlikely. The close temporal relationship between the initiation of tirzepatide and the onset of obsessive–compulsive symptoms suggests a possible causal link. The absence of any prior psychiatric history or obsessive–compulsive traits, the improvement of symptoms after drug discontinuation, and the lack of other pharmacological explanations further support this relationship.

Given that tirzepatide can affect the central nervous system through multiple pathways—and that GLP-1 receptor activation interacts with dopaminergic and

serotonergic systems—it is possible that this event reflects an idiosyncratic susceptibility. Although neuropsychiatric adverse effects such as depression, anxiety, and suicidal ideation have been reported with GLP-1 receptor agonists, the development of obsessive–compulsive symptoms has not been previously described.

To our knowledge, this is the first case in the literature reporting the development of obsessive–compulsive disorder associated with tirzepatide use. Further studies are needed to clarify this potential relationship.

Given that similar cases may appear in the future, this reaction may eventually need to be reflected in the drug's safety information. Patients and caregivers should be informed about the potential onset of obsessive–compulsive thoughts or behaviors during treatment. This case has been reported to the Turkish Pharmacovigilance Center (TÜFAM).

CONCLUSION

Tirzepatide is an injectable dual GIP and GLP-1 receptor agonist used in the management of obesity and T2DM. While gastrointestinal side effects are the most common, clinicians should also be aware of the potential for rare psychiatric adverse events, such as OCD. Early recognition and appropriate management of such effects can improve treatment adherence and overall outcomes.

Ethical Considerations

Ethical approval

Ethical approval was not required for this single-patient case report, in accordance with local regulations.

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Conflict of Interests

The authors declare that they have no conflicts of interest.

Data availability

A All data generated or analyzed during this case are included in this published article.

Patient consent

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

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