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Case Report / Olgu Sunumu

Severe Diarrhea Following Tirzepatide Therapy in a Woman with Celiac Disease

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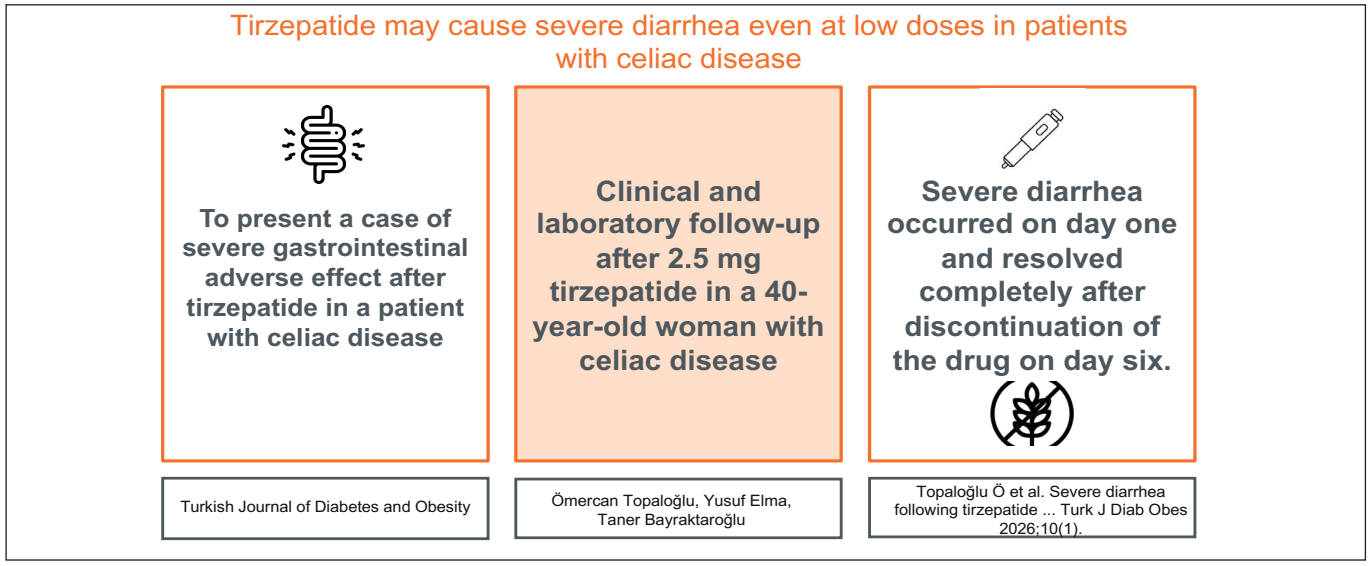
GRAPHICAL ABSTRACT



ABSTRACT

Tirzepatide, a dual agonist of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, has demonstrated marked efficacy in glycemic control and weight reduction but is frequently associated with gastrointestinal adverse effects. Data on its safety in patients with celiac disease are limited. We describe a 40-year-old woman with well-controlled celiac disease on a strict gluten-free diet who developed severe watery diarrhea immediately after the first 2.5 mg dose of tirzepatide, initiated for weight management. She experienced up to ten diarrheal episodes per day with dehydration and fatigue, requiring intravenous fluid replacement. Laboratory evaluation revealed mild hypokalemia and elevated AST. No infectious or dietary triggers were identified. Tirzepatide was discontinued, resulting in complete symptom resolution. Gastrointestinal intolerance is a known dose-dependent adverse effect of tirzepatide; however, such acute and severe reactions at the starting dose are uncommon. The coexistence of celiac disease may have increased susceptibility to enteric side effects through altered intestinal mucosal or immune mechanisms. This case highlights the potential for severe gastrointestinal intolerance to tirzepatide, even at low doses, in patients with celiac disease. Careful monitoring and individualized risk assessment are recommended when prescribing tirzepatide to patients with pre-existing gastrointestinal disorders.

Keywords: *Celiac disease, Diarrhea, Gastrointestinal adverse effects, GLP-1 receptor agonist, Weight management*

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Çölyak Hastalığı Olan Bir Kadında Tirzepatid Tedavisi Sonrası Gelişen Şiddetli Diyare

GRAFİKSEL ÖZET

ÖZ

Glukagon benzeri peptid-1 (GLP-1) ve glukoz bağımlı insülinotropik polipeptid (GIP) reseptörlerinin dual agonisti olan Tirzepatid, glisemik kontrol ve kilo kaybında belirgin etkinlik göstermiştir ancak sıklıkla gastrointestinal yan etkilerle ilişkilendirilmektedir. Çölyak hastalığı olan hastalarda kullanımına ilişkin güvenlik verileri sınırlıdır. Kilo yönetimi amacıyla başlanan 2,5 mg'lık ilk tirzepatid dozundan hemen sonra şiddetli sulu diyare gelişen, sıkı bir glutensiz diyetle kontrol altında olan 40 yaşında bir kadın çölyak hastasını sunuyoruz. Hasta, dehidrasyon ve halsizliğin eşlik ettiği, intravenöz sıvı replasmanı gerektiren, günde on keze varan diyare atakları yaşamıştır. Laboratuvar değerlendirmesinde hafif hipokalemi ve yüksek AST saptanmıştır. Herhangi bir enfeksiyöz veya diyetsel tetikleyici tanımlanmamıştır. Tirzepatid tedavisi sonlandırılmış ve semptomlar tamamen düzelmiştir. Gastrointestinal intolerans, tirzepatidin bilinen ve doza bağlı bir yan etkisidir ancak başlangıç dozunda bu denli akut ve şiddetli reaksiyonlar nadirdir. Mevcut çölyak hastalığı, değişmiş bağırsak mukozası veya immün mekanizmalar yoluyla enterik yan etkilere duyarlılığı artırmış olabilir. Bu olgu, çölyak hastalarında düşük dozlarda bile tirzepatide karşı şiddetli gastrointestinal intolerans potansiyelini vurgulamaktadır. Önceden var olan gastrointestinal bozukluğu olan hastalara tirzepatid reçete edilirken dikkatli izlem ve bireyselleştirilmiş risk değerlendirmesi önerilir.

Anahtar Sözcükler: *Çölyak hastalığı, Diyare, Gastrointestinal yan etkiler, GLP-1 reseptör agonisti, Kilo yönetimi*

INTRODUCTION

Tirzepatide is a dual agonist of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) receptors, approved for the treatment of type 2 diabetes and investigated for obesity management. It has shown substantial efficacy in improving glycemic control and inducing significant weight reduction (1,2). However, gastrointestinal adverse effects—including nausea, vomiting, diarrhea, reduced appetite, constipation, and abdominal discomfort—are common and appear to increase with higher doses (2,3). High-dose regimens, such as 10–15 mg weekly, are associated with greater discontinuation rates compared with lower doses or other GLP-1 receptor agonists (4). Celiac disease is an immune-mediated enteropathy triggered by gluten exposure, characterized by villous atrophy and intestinal malabsorption. Clinical manifestations include diarrhea, weight loss, and nutritional deficiencies. Because GLP-1 receptor agonists influence gastrointestinal motility and nutrient absorption, their use in patients with celiac disease warrants careful monitoring.

Retrospective evidence suggests that patients with celiac disease receiving anti-obesity medications, including GLP-1 receptor agonists, achieve weight loss outcomes and gastrointestinal side-effect rates similar to those without celiac disease (5). Nevertheless, tirzepatide-related adverse events predominantly involve the gastrointestinal tract and are

most likely to occur within the first six months of therapy (6). This report describes a case of severe, tirzepatide-associated diarrhea in a woman with celiac disease, leading to treatment discontinuation.

CASE REPORT

Written informed consent was obtained from the participant. A 40-year-old woman presented with weight gain and postprandial fatigue. Her past medical history included Hashimoto's thyroiditis, celiac disease, rosacea, and lichen sclerosus. She adhered strictly to a gluten-free diet. Despite multiple attempts with lifestyle intervention, she was unable to achieve weight loss. Her medications included oral levothyroxine (75 mcg daily, six days per week, and 100 mcg once weekly) and topical glucocorticoids. She reported an allergy to naproxen sodium. Surgical history was significant for a cesarean section and lipoma excision from the left arm. On examination, she appeared well. Weight was 78.4 kg, height 166 cm (BMI 28.5 kg/m^2), and waist circumference 98 cm. Systemic examination was unremarkable. Electrocardiography revealed sinus rhythm at 65 bpm. Laboratory findings were within reference ranges: ALT 15 U/L, AST 21 U/L, GGT 14 U/L, ALP 69 U/L, creatinine 0.89 mg/dL, Na 139 mEq/L, K 4.5 mEq/L, LDL 125 mg/dL, HDL 59 mg/dL, total cholesterol 198 mg/dL, triglycerides 70 mg/dL, fasting glucose 80 mg/dL, HbA1c 5.5%, TSH 4.68 mIU/L, free T4 0.72 ng/dL. Abdominal ultrasound showed grade 1 hepatic steatosis. Thyroid ultrasound revealed a heterogeneous parenchymal pattern. Based on overweight and hepatic steatosis, and given the willingness of the patient and the absence of contraindications, weekly subcutaneous tirzepatide 2.5 mg was initiated alongside dietary counseling. Her levothyroxine dose was adjusted to 87.5 mcg daily. On day one of tirzepatide, she developed profuse watery diarrhea, up to ten episodes per day, accompanied by fatigue and dehydration but without nausea or vomiting. By day six, she presented with persistent symptoms. Blood pressure was 100/65 mmHg and heart rate 97 bpm. She received two liters of intravenous isotonic saline over four hours. Laboratory evaluation showed ALT 13 U/L, AST 58 U/L, GGT 13 U/L, ALP 72 U/L, creatinine 0.94 mg/dL, Na 135 mEq/L, K 3.6 mEq/L, and fasting glucose 65 mg/dL. Tirzepatide was discontinued, after which diarrhea resolved promptly. She continues follow-up under close monitoring.

DISCUSSION

This case describes a woman with celiac disease who developed intractable diarrhea immediately following initiation of tirzepatide therapy. Given the severity of her symptoms and biochemical evidence of dehydration, the drug was discontinued with subsequent clinical improvement. To our knowledge, this is the first report describing severe gastrointestinal intolerance to tirzepatide in a patient with celiac disease. Tirzepatide and other GLP-1 receptor agonists are known to induce gastrointestinal side effects, typically in a dose-dependent fashion (7). Previous reports include cases of severe nausea, vomiting, diarrhea, abdominal pain, and even acute kidney injury necessitating hospitalization (8). Retrospective analyses suggest that celiac patients and non-celiac individuals exhibit comparable efficacy and tolerability with GLP-1 receptor agonists such as liraglutide and semaglutide (5). However, data specifically addressing tirzepatide in this subgroup remain scarce.

Interestingly, a rare report documented tirzepatide-associated duodenal villous blunting and chronic inflammatory changes resembling celiac disease histologically, which resolved after drug withdrawal (9). Such observations highlight the need to differentiate drug-induced enteropathy from primary celiac disease in clinical practice. A recent observational study further emphasized that tirzepatide-related adverse reactions most frequently involve the gastrointestinal tract, often within the first six months of treatment (6). In our case, however, severe diarrhea occurred on the very first day of exposure.

Conclusion

This report illustrates a case of tirzepatide-induced severe diarrhea in a patient with celiac disease, necessitating treatment discontinuation. Even at the lowest approved starting dose, tirzepatide may provoke acute gastrointestinal intolerance in susceptible individuals. Clinicians should be vigilant for early gastrointestinal adverse effects, particularly in patients with pre-existing gastrointestinal conditions such as celiac disease. Personalized monitoring and individualized therapeutic strategies are warranted, and further studies are needed to establish the safety profile of tirzepatide in this population.

Author's Contributions

Ömercan Topaloğlu conceptualized this article. **Ömercan Topaloğlu** and **the other two authors** contributed the writing and submission processes. **Taner Bayraktaroğlu** did not participate in the evaluation and decision-making processes for this publication.

Conflict of Interest

All authors have declared no conflicts of interest. This case was presented as a poster presentation at 23-26 October 2025 in Endobridge congress in Antalya.

Peer Review Process

Extremely and externally peer-reviewed .

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