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CASE REPORT

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Massive Pericardial Effusion as a Rare Complication of Semaglutide Therapy

Semaglutid Tedavisine Bağlı Nadir Bir Komplikasyon: Masif Perikardiyal Efüzyon

Tuğba Çetin[1]*, Fahri Çakan[2], Levent Pay[3]

1.Department of Cardiology, Tekirdağ Çorlu State Hospital, Tekirdağ, Türkiye
2.Department of Cardiology, Alanya Alaaddın Keykubat Unıversıty, Faculty of Medıcıne, Antalya, Türkiye
3.Department of Cardiology, Istanbul Çam and Sakura Hospital, Istanbul, Türkiye

ABSTRACT

In this report, we present a case of a 35-year-old woman presenting with abdominal distension, leg edema, and abdominal pain shortly after initiating weekly subcutaneous injections of semaglutide (Ozempic®) 0.5 mg. Imaging and transthoracic echocardiography identified significant pericardial effusion and pericardiocentesis yielded approximately 1000 cc of serohemorrhagic fluid. Cytological analysis showed no evidence of malignancy or infection. Routine laboratory investigations were unremarkable except for a transient elevation of serum CA-125. At 3-month follow-up, she remained asymptomatic with no recurrence of pericardial effusion. This case highlights massive pericardial effusion as a rare potential side effect of semaglutide and underscores the importance of regular monitoring for cardiac adverse effects during semaglutide therapy.

Keywords: drug-related side effect; pericardial effusion; semaglutide.

ÖZ

Bu yazıda, haftalık 0,5 mg subkutan semaglutid (Ozempic®) enjeksiyonlarına başlanmasından kısa bir süre sonra abdominal distansiyon, bacak ödemi ve karın ağrısı gelişen 35 yaşındaki bir kadın olgusu sunuldu. Görüntüleme ve transtorasik ekokardiyografi ile belirgin perikardiyal efüzyon saptandı. Yapılan perikardiyosentez ile yaklaşık 1000 cc serohemorajik sıvı drene edildi. Sitolojik analizde malignite veya enfeksiyon bulgusuna rastlanmadı. Serum CA-125 düzeyindeki geçici yükseklik dışında rutin laboratuvar bulguları normal sınırlarda değerlendirildi. Üç aylık takipte, hastanın asemptomatik olduğu ve perikardiyal efüzyonun tekrarlamadığı görüldü. Bu olgu, semaglutid kullanımına bağlı olarak gelişebilecek nadir bir yan etki olan perikardiyal efüzyonu ve semaglutid tedavisi sırasında kardiyak advers etkiler açısından düzenli izlemin önemini ortaya koymaktadır.

Anahtar Kelimeler: ilaca bağlı yan etki; perikardiyal efüzyon; semaglutid.

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*Corresponding Author: Tuğba Çetin. MD. Department of Cardiology, Tekirdağ Çorlu State Hospital. Tekirdağ, Türkiye. Phone: +90- 282 693 33 00 / mail: drtugbacetin@gmail.com

ORCID: 0000-0001-8555-988X

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Introduction

In recent years, the use of sodium-glucose cotransporter-2 inhibitors (SGLT2 inhibitors) or glucagon-like peptide-1 receptor agonists (GLP-1RA) has been increasingly adopted in the management of obese patients with type 2 diabetes, due to their dual benefits of improving glycaemic control and promoting weight loss. SGLT2 inhibitors prevent glucose reabsorption in the renal proximal tubules, thereby contributing to glycaemic control [1]. In contrast, GLP-1RA promote insulin secretion in response to elevated glucose levels and suppress glucagon release after meals [2]. Recently, semaglutide (Ozempic®) has gained considerable popularity as a GLP-1RA that is widely used to promote weight loss. We present a case of massive pericardial effusion as a rare adverse effect potentially associated with semaglutide.

Case Report

A 35-year-old woman presented to the emergency department with complaints of abdominal distension, leg swelling, and abdominal pain. Approximately 9 months earlier, she had visited the internal medicine outpatient clinic seeking support for weight loss. She was started on empagliflozin 10 mg /day (Forziga□), but due to insufficient benefit, semaglutide was introduced three months prior to admission. She reported receiving weekly injections of semaglutide 0.5 mg resulting in weight reduction of approximately 13 kilograms during this period. Her current symptoms began shortly after starting semaglutide and progressively intensified. She reported no history of alcohol or illicit drug use. At the time of admission, her vital signs revealed a blood pressure of 122/82 mmHg and a regular heart rate of 117 bpm. Oxygen saturation was 95% on room air. The admission electrocardiogram demonstrated sinus tachycardia. Laboratory findings revealed an elevated CA-125 level of 289 U/mL, while all other cancer markers were normal. In addition, inflammatory parameters—including white blood cell count and C-reactive protein—as well as thyroid function tests were all within normal ranges. Transthoracic echocardiography (TTE) revealed a normal left ventricular ejection fraction (LVEF) of 60%, along with a large pericardial effusion (shown in Figure 1A–B). Marked respiratory variation in mitral and tricuspid inflow velocities (shown in Figure 2A–B) as well as a constant dilated inferior vena cava (IVC) without any respiratory change (shown in Figure 3A) were observed—findings consistent with echocardiographic features of cardiac tamponade. Following initial evaluation, the patient was admitted to the Coronary Intensive Care Unit (CICU), and routine laboratory investigations were performed. Following informed consent, pericardiocentesis was performed through a subcostal approach, yielding approximately 1000 cc of fluid that was initially serohemorrhagic in nature (shown in Figure 3B) but later transitioned to a more serous appearance (shown in Figure 3C). The fluid was considered to be transudate (LDH gradient:0.50, protein gradient:0.46, glucose:96mg/dl). As the pericardial effusion decreased over the next three days, the catheter was subsequently removed. Post-procedure TTE demonstrated complete resolution of the pericardial effusion (shown in Figure 1C-D), normalization of respiratory variations in the mitral and tricuspid inflow velocities (shown in Figure 2C-D) and collapsible IVC (shown in Figure 3D). Consultations were requested from oncology, general surgery and gynaecology departments. Based on their recommendations, abdominal and pelvic ultrasonography, abdominal and pelvic computed tomography (CT) and thoracic CT were performed. The elevated CA-125 was thought to be related to pleural and pericardial effusion and fluid accumulation in the body; during follow-up, the levels returned to the normal range. Cytological analysis of the pericardial fluid demonstrated reactive mesothelial cells, lymphocytes, and rare neutrophils with no atypical cells observed, and the adenosine deaminase test was negative. The acid-resistant bacilli test was also negative. In light of these findings, consultations were obtained from oncology, general surgery and gynaecology departments, and no evidence of malignancy was detected. The patient was discharged in a stable condition without any complaints. Semaglutide therapy was permanently discontinued after hospitalization, and the patient was not re-exposed to the drug because of the suspected drug-related adverse event. At the 6-month follow-up, she remained asymptomatic and repeat

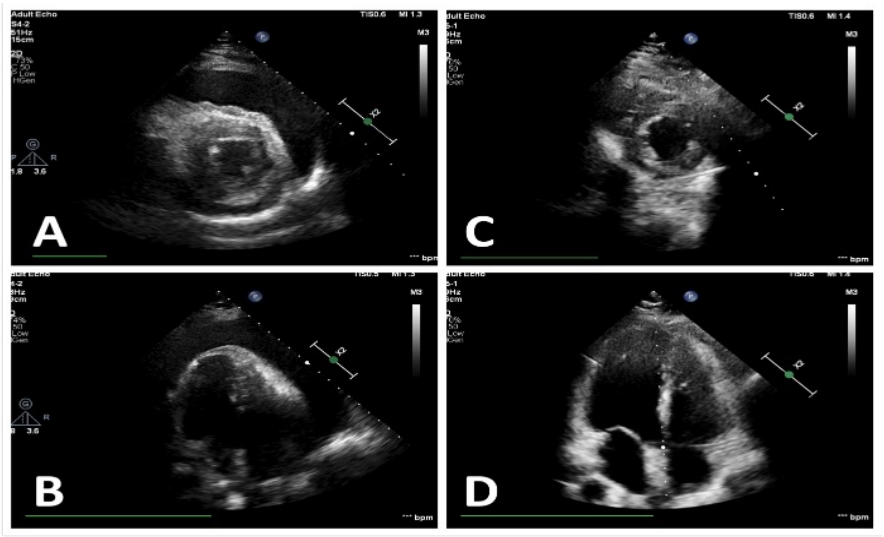


Figure 1 (A)(B) Pre-procedure two-dimensional transthoracic echocardiography (2D TTE) in short-axis and four-chamber views demonstrating a massive pericardial effusion (indicated between the blue arrows). (C)(D) Post-procedure 2D TTE in short-axis and four-chamber views showing a massive pericardial effusion.

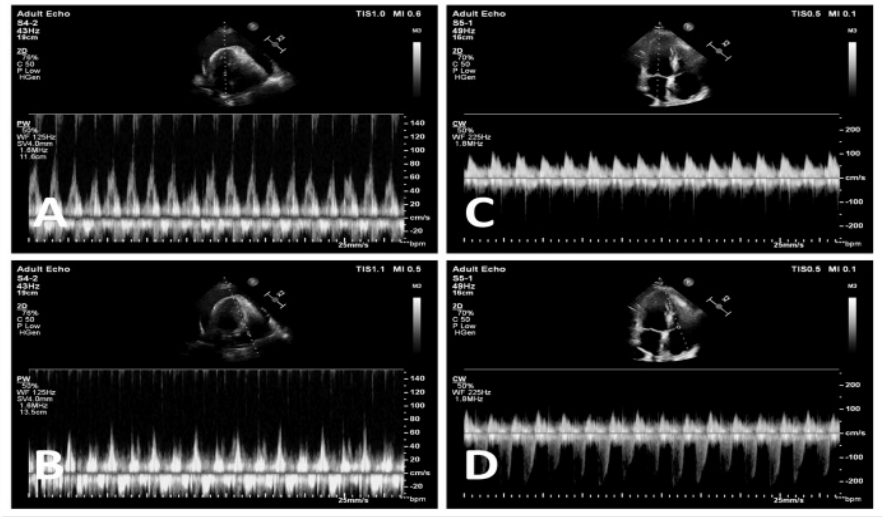


Figure 2 (A)(B) Pre-procedure 2D TTE in four-chamber views demonstrating increased mitral and tricuspid inflow sequentially. (C)(D) Post-procedure 2D TTE in four-chamber views demonstrating mitral and tricuspid inflow sequentially.

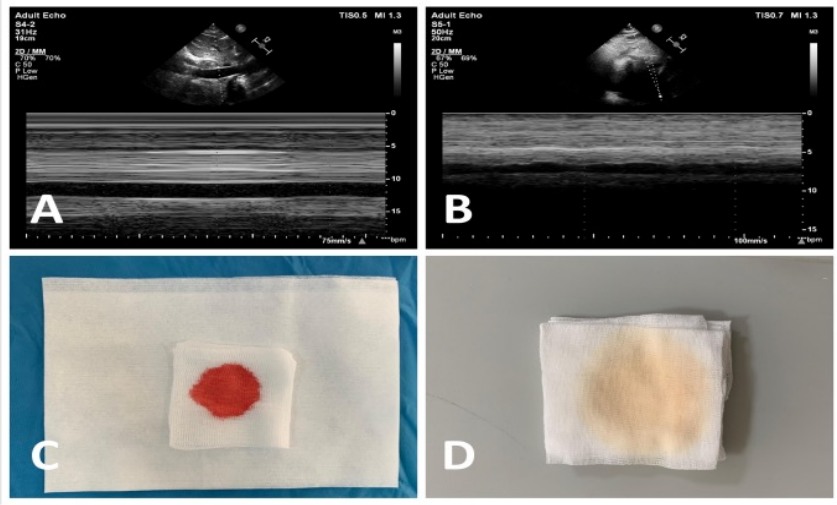


Figure 3. Pre- and post-procedural 2D TTE in subcostal view demonstrating a markedly dilated IVC (A) and a fully collapsible IVC following pericardiocentesis (B). Pericardial drainage fluid initially serohemorrhagic in appearance (C), later transitioning to a more serous character (D).

transthoracic echocardiography demonstrated no evidence of recurrent pericardial effusion. She was subsequently scheduled for routine clinical follow-up.

Discussion

Massive pericardial effusion is a rare but potentially life-threatening clinical condition that may be associated with semaglutide therapy. Although uncommon, clinicians should consider this diagnosis in patients receiving semaglutide who present with dyspnea, palpitations, or other symptoms suggestive of pericardial involvement.

Adverse effects associated with semaglutide have been increasingly recognized as its clinical use expands. The most frequently reported side effects are gastrointestinal, including nausea, vomiting, bloating, and, in more severe cases, even gastroparesis [3]. Beyond these common complaints, several case reports have documented rare but serious adverse events. According to a recently published case report, the initiation of semaglutide in a patient with schizophrenia who was being treated with ziprasidone resulted in decreased serum levels of ziprasidone and a subsequent worsening of paranoid delusions [4]. Furthermore, there are case reports in the literature describing semaglutide-induced lupus erythematosus with multiorgan involvement, diabetic ketoacidosis and acute pancreatitis however there have been no reports linking semaglutide to pericardial effusion which makes this case clinically significant [5-7].

Clinical trials evaluating the cardiovascular outcomes of semaglutide and empagliflozin have demonstrated that both medications significantly reduce the risk of major adverse cardiovascular events (MACE) including cardiovascular death, myocardial infarction and stroke [8]. Chen et al. evaluated drug-related adverse events-including diabetic ketoacidosis, urinary tract infection, acute pancreatitis and intestinal obstruction- as safety outcomes and reported no significant differences between GLP-1RA and SGLT2i therapies [6]. Saeed et al. demonstrated that the addition of a semaglutide to an empagliflozin was associated with lower rates of death, myocardial infarction, or stroke compared to empagliflozin monotherapy, with no significant differences in drug-related side effects between the groups [9].

Cardiac tamponade may result from a variety of aetiologies, including malignancies, uraemia secondary to chronic kidney disease, and infectious pericarditis—particularly of viral or tuberculous origin. Additionally, iatrogenic causes following cardiac procedures, trauma (both blunt and penetrating), and certain medications or drug reactions may also contribute [10]. In our patient, comprehensive evaluations including consultations with internal medicine and oncology specialists, laboratory tests, and imaging studies revealed no evidence suggestive of an underlying malignancy. Infectious markers were within normal limits, and there were no clinical or laboratory findings indicative of an active infection or tuberculosis. The patient had no history of recent trauma, and thyroid function tests were normal. After excluding other potential underlying aetiologies and considering the temporal relationship between the initiation of semaglutide therapy and the onset of symptoms, we concluded that semaglutide was the most likely cause of the cardiac tamponade in this case.

Cardiac tamponade may represent a rare complication associated with semaglutide either as monotherapy or in combination with SGLT2i. Although semaglutide and SGLT2i have demonstrated remarkable cardiovascular benefits in clinical trials, there remains a lack of well-established guidelines for routine cardiac monitoring during their use. It is critical to develop cardiac follow-up protocols, particularly for patients with preexisting cardiovascular conditions, those receiving multiple antidiabetic agents and those presenting with new-onset cardiac symptoms to ensure early detection of potentially serious adverse events. Further research is needed to better define the incidence, mechanisms and risk factors associated with semaglutide-related cardiac complications.

Conclusions

In summary, although semaglutide is known for its cardiovascular benefits, clinicians should be aware of serious adverse cardiac events. While routine cardiac monitoring is not currently recommended for all patients receiving semaglutide, clinicians should consider appropriate cardiac evaluation

in patients who develop new cardiovascular symptoms, including shortness of breath, leg swelling, or palpitations, as these may indicate underlying pericardial involvement.

Conflict of Interest Statement: The authors have no conflict of interest to declare.

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Data Availability Statement: All data generated or analyzed during this case are included in the article. No additional datasets were generated or analyzed.

Ethical Committee Approval and Informed Consent Statements: The study followed the ethical principles outlined in the 1964 Declaration of Helsinki and its later amendments. Informed consent form for case presentation was obtained from the patient and her relatives. All relevant data are within the paper and its Supporting Information files.

Use of AI statement: No artificial intelligence (AI) or AI-assisted technologies were used in the preparation of this study.

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Declaration of congress abstract: This study has not been presented at any national or international scientific meeting as an oral or poster presentation.

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