AUCTORES
Globalize your Research

Journal of Clinical Case Reports and Studies

Meenu Singh *

Open Access

Case Report

From Glycaemic Control to Gastrointestinal Crisis: A Case of Semaglutide-Induced Pancreatitis

Rutvik Jadvani and Meenu Singh*

Department of General Internal Medicine, University of Utah School of Medicine, Salt Lake City, Utah, USA.

***Corresponding Author:** Meenu Singh, University of Utah School of Medicine, Division of General Internal Medicine, University of Utah Health Salt Lake City, Utah, USA.

Received date: June 20, 2025; **Accepted date:** June 27, 2025; **Published date:** July 04, 2025

Citation: Rutvik Jadvani and Meenu Singh, (2025), From Glycaemic Control to Gastrointestinal Crisis: A Case of Semaglutide-Induced Pancreatitis, *J, Clinical Case Reports and Studies*, 6(5); **DOI:10.31579/2690-8808/265**

Abstract

Acute pancreatitis is a common illness usually secondary to gallstones, alcohol consumption, and hypertriglyceridemia. Less common causes include drug-induced pancreatitis. Semaglutide, a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist, is a novel agent for the treatment of type 2 diabetes mellitus (T2DM), obesity, and cardiovascular disease (CVD) risk reduction in diabetics, with documented gastrointestinal side effects but an extremely rare association with pancreatitis. We report a case of a 68-year-old female with a history of T2DM, obesity, and hypertension who experienced acute pancreatitis following the start of semaglutide 0.5 mg once weekly for one month. The patient also had a possible history of pancreatitis after taking exenatide and liraglutide. The patient presented with intense epigastric pain, nausea, and bloating, with increased lipase levels. Imaging evaluation did not reveal evidence of gallstones or pancreatic inflammation. Since there was a temporal correlation between starting semaglutide and the development of symptoms, the drug was withheld, and the patient responded to supportive measures with intravenous hydration and management of pain. This case highlights possible association of semaglutide with pancreatitis. Prompt recognition of possible association and drug cessation are essential for the best possible outcomes. More research is required to understand the association between semaglutide and pancreatitis and an underlying pathophysiology to develop improved guidelines for safe use.

Key Words: acute pancreatitis; semaglutide; glucagon-like peptide-1 (GLP-1); lipase

Introduction

Acute pancreatitis is an inflammatory process of the pancreas [1]. It usually presents with the abrupt onset of epigastric or diffuse abdominal pain, nausea, vomiting, and abdominal distention with increased serum pancreatic enzymes like amylase and lipase [2]. The most frequent etiologies of acute pancreatitis are gallstones, alcohol abuse, obesity, hypertriglyceridemia, hypercalcemia, endoscopic retrograde cholangiopancreatography (ERCP), intraductal papillary mucinous tumor, and drug-induced pancreatitis [1,2]. Drug-induced pancreatitis is a significant but less well-known etiology [2]. There have been several medications implicated in acute pancreatitis development, including specific classes of medication such as diuretics, corticosteroids, antiretrovirals, antiepileptics, antibiotics, and immunosuppressants [2]. Among newer medications, glucagon-like peptide-1 (GLP-1) receptor agonists, eg, semaglutide, have recently received attention with suspected adverse gastrointestinal manifestations, including pancreatitis [3].

Semaglutide, glucagon-like peptide-1 (GLP-1) agonist, was first approved in 2017 by the U.S. Food and Drug Administration (FDA) for the treatment of T2DM, weight management in non-diabetic individuals, and cardiovascular disease (CVD) risk reduction in diabetic individuals. It is a popular choice for the treatment of obesity and T2DM, especially in those who have not been optimally controlled with other treatments [4,5]. Marso SP et al. found that semaglutide-treated patients had a significant 26% (semaglutide 6.6% vs. placebo 8.9%) lower risk of the primary composite outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke [6]. Semaglutide increases glucose-dependent insulin secretion, inhibits glucagon release, and delays gastric emptying, all of which help to achieve better glycemic control and weight loss [7]. It can be given daily by oral (PO) and weekly by subcutaneously (SQ) routes, however because of pharmacokinetics difference SQ route is preferred [8].

In spite of its therapeutic effect, semaglutide is also linked to a variety of side effects, the most frequent of which being gastrointestinal (GI) symptoms including nausea, vomiting, constipation, and diarrhea in nearly one-fifth of all patients treated with semaglutide [3]. Less common GI side effects include pancreatitis, gastroparesis, bowel obstruction, and gallstones. Pancreatitis associated with GLP-1 receptor agonists has also evoked concerns regarding the safety of the class of drugs [9, 10]. In literature, numerous cases have been reported of acute pancreatitis after initiating semaglutide for type 2 diabetes mellitus and obesity [12,13,14]. Here we

report one such case of acute pancreatitis likely secondary to the use of semaglutide.

Case Presentation

The patient is a 68-year-old female with a medical history significant for type 2 diabetes mellitus, hypertension, obesity, and breast cancer. Patient reported a possible history of pancreatitis after taking exenatide and liraglutide which resolved after discontinuation. Long-standing outpatient medications consisted of dapagliflozin 10 mg once daily, losartan-hydrochlorothiazide 125 mg once daily, bupropion XL 150 mg once daily, atorvastatin 20 mg once daily, potassium chloride 40 mg once daily, citalopram 20 mg once daily, sitagliptin 100 mg once daily, metoprolol succinate ER 25 mg once daily, insulin glargine and semaglutide 0.5 mg once weekly since one month prior.

She presented to the emergency department with complaints of intense nausea, bloating, and sudden onset sharp stabbing abdominal pain (10/10) in the epigastrium with radiation to her back. She was able to pass gas and decreased bowel movement. The patient denied any alcohol use, tobacco use, recreational drug use, recent abdominal injury or chronic abdominal pain. Past surgical history was significant for cholecystectomy and double mastectomy for breast cancer. All vitals were within normal ranges except that tachycardia due to acute pain. On examination, she was in acute pain and moaning. The abdomen was soft, mild epigastric tenderness, distended, and decreased bowel sounds. The rest of the physical examination was unremarkable.

Complete blood count (CBC) was notable for white blood cell count of 13.26 (normal range: 4.30 - 11.30 k/uL) and neutrophils of 10.69 (normal range: 2.00 - 7.40 k/uL). Complete metabolic panel (CMP) was unremarkable, aside from the elevated lipase level of 1,189 (normal range: 10-140 U/L), potassium level of 3.1 (normal range: 3.3 - 5.0 mmol/L), anion gap of 22 (normal range: 8 - 14 mmol/L), creatinine level of 1.17 (normal range: 0.57 - 1.11 mg/dL) and glucose level of 195 (normal range: 64 - 128 mg/dL). Lipid panel, lactic acid, and liver function tests were unremarkable. Computed tomography (CT) of the abdomen and pelvis with intravenous contrast revealed normal-appearing pancreas without inflammation and previous cholecystectomy with expected postoperative mild intrahepatic biliary ductal dilatation. For acute pancreatitis, there are 3 diagnostic criteria which include abdominal pain in the epigastric region, elevated lipase level, and CT findings. However, for the diagnosis, only 2 of them are required. In our patient, 2 of 3 diagnostic criteria was considered for diagnosing acute pancreatitis.

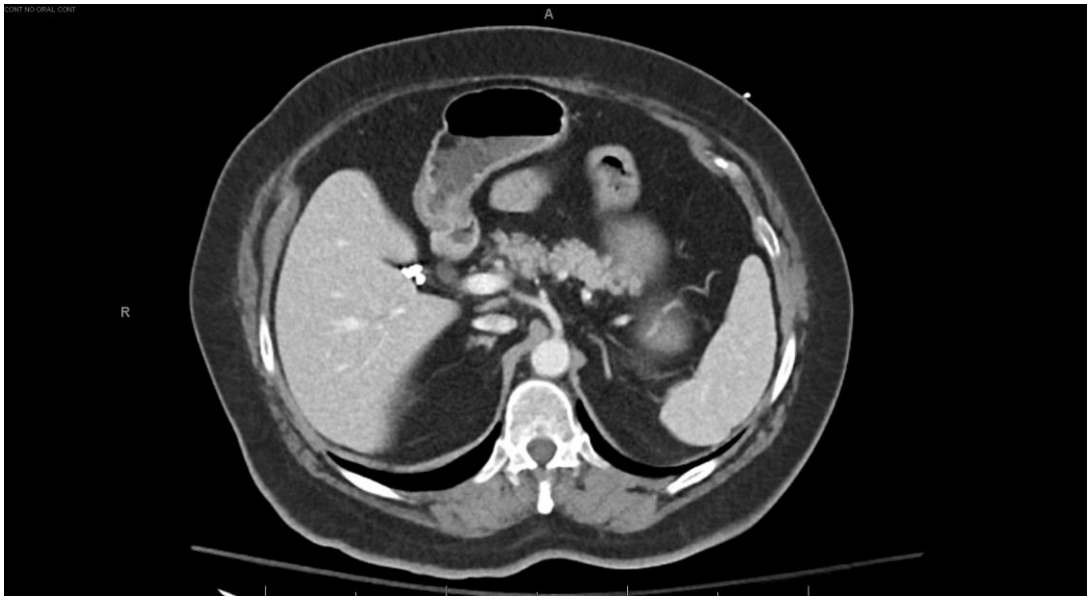

Figure 1: Computed tomography (CT) scan of the abdomen and pelvis with contrast revealed normal-appearing pancreas without inflammation.

Lab Result	Lab Value	Normal Range
WBC	13.26	4.30 - 11.30 k/uL
Neutrophil %	80.6	39.4 - 72.5 %
Neutrophil #	10.69	2.00 - 7.40 k/uL
Lipase	1,189	8 - 78 U/L
Lactic Acid	1.9	0.5 - 2.2 mmol/L
Potassium	3.1	3.3 - 5.0 mmol/L
Calcium	9.8	8.4 - 10.5 mg/dL
Creatinine	1.17	0.57 - 1.11 mg/dL

Glucose	195	64 - 128 mg/dL
Anion Gap	22	8 - 14 mmol/L
Total Bilirubin	0.8	0.2 - 1.4 mg/dL
Alkaline Phosphatase	102	38 - 126 U/L
AST	27	16 - 40 U/L
ALT	19	5 - 60 U/L
Lipid Panel		
Lab Result	**Lab Value**	**Normal Range**
Total Cholesterol	164	< 200 mg/dL
Triglycerides	115	30 - 149 mg/dL
LDL Cholesterol, Calc	100	0 - 129 mg/dL
VLDL, Calc	23	0 - 30 mg/dL
Non-HDL Cholesterol	123	< 130 mg/dL
HDL Cholesterol	41	40 - 59 mg/dL

Table 1: Laboratory Values

Given the suspicion of acute pancreatitis and the timing associated with semaglutide initiation, administration of the drug was discontinued. Her symptoms resolved and lipase and white blood cell count levels normalized within days of semaglutide discontinuation and conservative treatment including continuous IV fluid administration and pain management. At her follow-up visit, she remains without recurrence of abdominal pain. And as per the literature she was advised not to rechallenge with semaglutide for safety reasons.

Discussion

GLP-1 receptor agonists are generally well tolerated and efficacious in the management of type 2 diabetes, obesity, and CVD risk reduction in diabetics [3,11]. Despite efficacy and popularity of this class of drugs, there are concerning side effects including pancreatitis [12,13,14]. The precise mechanism by which semaglutide and other GLP-1 receptor agonists cause pancreatitis is unclear.

One potential mechanism is that GLP-1 receptor agonists directly affect pancreatic β-cells. GLP-1 receptors are located on pancreatic cells, and while stimulation of these receptors benefits insulin release, stimulation is also theorized to cause overstimulation leading to β-cell damage or dysfunction [15]. However, in a case-control study by Thomsen RW et al., the risk of acute pancreatitis in patients was not increased among GLP-1 receptor agonist users compared with nonusers (OR 0.82 [95% CI 0.54–1.23]) [16]. Case reports of pancreatitis induced by semaglutide have also emphasized the requirement for careful monitoring of these patients. For instance, one case published by Patel F et al. had a patient who developed acute pancreatitis following the initiation of semaglutide, with an identical clinical presentation to our case, such as dose and duration of semaglutide use, increased lipase levels, negative CT findings, stopping semaglutide resulted in a resolution of symptoms, and recommendation to not restart [12].

This patient, who started weekly semaglutide 0.5 mg one month prior, did not report the typical history associated with acute pancreatitis, such as alcohol use, abdominal trauma, steroid use, viral infection, gallstones, or autoimmune disease. In addition to that, laboratory workup was negative for hypercalcemia and hypertriglyceridemia. Also, the patient was on other possible drugs that can cause pancreatitis since quite some time. The combination of recent semaglutide use, lack of classic history findings of acute pancreatitis, remarkably elevated lipase levels, point towards subcutaneous semaglutide as the most likely perpetrator of this patient's acute pancreatitis. The treatment of acute pancreatitis secondary to semaglutide is supportive care, such as intravenous hydration, analgesia, and electrolyte management. From the cases reported in the literature, it is important to discontinue the drug immediately [12,13,14]. Dagher C et al. reported severe acute pancreatitis secondary to semaglutide leading to cardiac arrest and death after four years of use with a dose increment four weeks prior to presentation [14]. Guo H et al. recommended that GLP-1RAs should not be restarted if pancreatitis is confirmed for safety reasons [17].

Here, semaglutide discontinuation led to the gradual improvement of the patient, and she was subsequently discharged without any late complications. Physicians must be keen to notice any sign of pancreatitis in semaglutide-treated patients, especially those with other risk factors like a history of pancreatitis, gallstones, or chronic alcoholism. Early identification and treatment are important in avoiding worse outcomes and complications.

Conclusion

Acute pancreatitis is an uncommon but potentially severe side effect of semaglutide treatment. Providers should be aware of this possible risk and carefully watch for pancreatitis signs and symptoms among patients taking GLP-1 receptor agonists. Early detection and timely treatment are essential to avoid significant consequences. With any drug, the advantages of semaglutide must be balanced against the risks, and the patients must be made aware of probable adverse effects. There is limited literature available on re-challenge with semaglutide, and further research is needed.

Financial interest

No financial interest

Conflict of interest

No conflict of interest

Disclosures

Nothing to disclose

Acknowledgments

We sincerely acknowledge and thank the University of Utah for the Laboratory investigation.

References:

1. Wang GJ, Gao CF, Wei D, Wang C, Ding SQ. (2009), Acute pancreatitis: etiology and common pathogenesis. *World J Gastroenterol*. Mar 28;15(12):1427-1430.
2. Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C, (2022), Acute Pancreatitis: Diagnosis and Treatment. Drugs. 82(12):1251-1276.
3. Smits MM, Van Raalte DH. (2021), Safety of Semaglutide. Front Endocrinol (Lausanne).12:645563.
4. Li A, Su X, Hu S, Wang Y. (2023), Efficacy and safety of oral semaglutide in type 2 diabetes mellitus: A systematic review and meta-analysis. *Diabetes Res Clin Pract*. 198:110605.
5. Trujillo JM, Nuffer W, Smith BA. (2021), GLP-1 receptor agonists: an updated review of head-to-head clinical studies. *Ther Adv Endocrinol Metab*. Mar 9;12:2042018821997320.
6. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al., (2016), SUSTAIN-6 Investigators. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med*. 375(19):1834-1844.
7. Drucker DJ. (2018), Mechanisms of Action and Therapeutic Application of Glucagon-like Peptide-1. Cell Metab. 27(4):740-756.
8. Kommu S, Whitfield P. (2025), Semaglutide. 2024 Feb 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
9. Giorda CB, Nada E, Tartaglino B, Marafetti L, Gnavi R. (2014), A systematic review of acute pancreatitis as an adverse event of type 2 diabetes drugs: from hard facts to a balanced position. *Diabetes Obes Metab*. 16(11):1041-1047.
10. Shetty R, Basheer FT, Poojari PG, Thunga G, Chandran VP, Acharya LD. (2022), Adverse drug reactions of GLP-1 agonists: A systematic review of case reports. *Diabetes Metab Syndr*. 16(3):102427.
11. Chao AM, Tronieri JS, Amaro A, Wadden TA. (2023), Semaglutide for the treatment of obesity. *Trends Cardiovasc Med*. 33(3):159-166.
12. Patel F, Gan A, Chang K, Vega KJ. (2023), Acute Pancreatitis in a Patient Taking Semaglutide. *Cureus*. 15(8): e43773.
13. Hughes K, Sumaruth YRK, Mohammed E, Sant Bakshsingh V. Acute Pancreatitis Likely Due to Semaglutide. Cureus. 2024 Sep 21;16(9): e69844.
14. Dagher C, Jailani M, Akiki M, Siddique T, Saleh Z, Nadler E. (2024), Semaglutide-Induced Acute Pancreatitis Leading to Death After Four Years of Use. *Cureus*. 16(9): e69704.
15. Røder ME. (2019), Clinical potential of treatment with semaglutide in type 2 diabetes patients. Drugs Context. 8:212585.
16. Thomsen RW, Pedersen L, Møller N, Kahlert J, Beck-Nielsen H, Sørensen HT. (2015), Incretin-based therapy and risk of acute pancreatitis: a nationwide population-based case-control study. *Diabetes Care*. 38(6):1089-1098.
17. Guo H, Guo Q, Li Z, Wang Z. (2024), Association between different GLP-1 receptor agonists and acute pancreatitis: case series and real-world pharmacovigilance analysis. *Front Pharmacol*. 15:1461398.

DOI:10.31579/2690-8808/265