



Semaglutide-Associated Severe Gastrointestinal Intolerance and Hepatic Granulomas: A Case Report

Authors: Aqsa Khan^{1*}, Badeeya Rashid¹, Fareedullah¹, Sibghatullah¹

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

***Corresponding Author:** aqsakhan023@gmail.com

DOI: <https://doi.org/10.66381/jod.2025.003>

Received: 13th September, 2025

Accepted: 02nd October, 2025

Published: 12th October, 2025



Abstract:

Background: Semaglutide (commonly known as Ozempic, Rybelsus, and Wegovy), a glucagon-like peptide-1 (GLP-1) receptor agonist. It is increasingly prescribed for diabetes and weight loss. While gastrointestinal side effects are well recognized, hepatic granulomas associated with its use have not been reported in the literature.

Case Presentation: A 36-year-old woman without comorbidities developed persistent nausea, early satiety, anorexia, diarrhea, and 5 kg weight loss within 4 weeks of starting semaglutide 0.25 mg weekly. Ultrasound imaging revealed multiple hepatic granulomas. Laboratory, infectious, and autoimmune evaluations were unremarkable. Following drug discontinuation, her symptoms resolved, and repeat imaging showed resolution of granulomas, eliminating the need for biopsy.

Discussion: This case highlights an atypical presentation of severe gastrointestinal intolerance and hepatic granulomas at a very low dose of semaglutide. The temporal association and resolution after withdrawal suggest a drug-induced hypersensitivity reaction or an immune dysfunction associated with its use.

Conclusion: Clinicians should remain alert for unusual adverse effects of semaglutide, even at initiation doses. Imaging and close follow-up are essential in cases with unexplained gastrointestinal symptoms and hepatic abnormalities.

Keywords: Semaglutide, GLP-1 receptor agonist, hepatic granulomas, gastrointestinal adverse effects



Introduction:

Semaglutide, a GLP-1 receptor agonist, has shown significant efficacy in type 2 diabetes and obesity management. By promoting satiety, delaying gastric emptying, and improving glycemic control, it is increasingly used off-label for weight loss. The most common adverse effects are gastrointestinal, including nausea, vomiting, and constipation. Drug-induced liver injury (DILI) has been reported but remains rare. Liver biopsy findings of one case report demonstrated features of acute hepatitis with mononuclear infiltrates and necrosis¹.

Contrary to liver injury associated with Semaglutide, studies have shown its potential for treating MASLD (metabolic syndrome-associated steatotic liver disease) and improving liver fibrosis².

To date, semaglutide-associated hepatic granulomas have not been well described in the literature. We report the case of a young woman who developed severe gastrointestinal intolerance and hepatic granulomas within four weeks of initiating low-dose semaglutide.

Case Presentation:

Patient Information

- **Age/Sex:** 36-year-old female

- **Medical history:** No prior comorbidities, no prior surgeries
- **Medications:** Initiated semaglutide 0.25 mg weekly for weight loss
- **Baseline weight/BMI:** 55 kg, BMI 21.5 kg/m²

Clinical Findings

After 4 weeks of therapy (fourth injection), the patient developed:

- Persistent nausea
- Early satiety
- Anorexia
- Diarrhea (new onset, baseline constipation)
- Sensation of food sticking in the oesophagus
- 5 kg weight loss (BMI dropped to 19.5 kg/m²)

She denied vomiting, abdominal pain, fever, jaundice, or gastrointestinal bleeding.

On examination:

- Vital signs stable, hydration adequate
- Mild epigastric tenderness
- No organomegaly
- Cardiovascular, respiratory, and neurological examinations normal

**Timeline:**

Event	Time (Weeks)	Findings/Management
Start semaglutide 0.25 mg weekly	Week 0	Weight 55 kg, BMI 21.5
After 4th injection	Week 4	Nausea, diarrhea, early satiety, 5 kg weight loss
Investigations	Week 4	Normal labs, US: hepatic granulomas
Discontinued semaglutide	Week 4	Started PPI, domperidone, diet modifications
Follow-up	Week 7	Symptoms improved, weight stable
Repeat ultrasound	Week 7	Resolution of hepatic granulomas
Liver biopsy	Deferred	Not required after resolution

Table 1: Timeline of Events

Diagnostic Assessment

- **Blood tests:** Normal CBC, ESR, CRP, LFTs, RFTs, thyroid profile
- **Stool tests & celiac serology:** Negative
- **Chest X-ray:** Clear
- **Ultrasound:** Multiple small hypoechoic granulomas in the liver
- **Infectious & autoimmune workup:** Pending at onset, no supportive findings later
- **Differential diagnosis:** Infectious granulomatous disease (TB, fungal), autoimmune hepatitis, sarcoidosis, drug-induced hypersensitivity

The strong temporal relationship with semaglutide initiation and spontaneous resolution following discontinuation supported a diagnosis of drug-induced hepatic granulomas.

Therapeutic Intervention

- Immediate discontinuation of semaglutide
- Supportive treatment: proton pump inhibitor, domperidone, dietary modifications
- Close clinical and radiological follow-up
- Liver biopsy was planned but ultimately deferred due to resolution of findings

Follow-Up and Outcomes

Within 3 weeks of drug discontinuation, the patient's gastrointestinal symptoms improved significantly. Repeat ultrasound demonstrated resolution of hepatic granulomas. Weight stabilized at 50 kg. She resumed her normal diet and daily activities.



Discussion:

GLP-1 receptor agonists are frequently associated with gastrointestinal adverse events, most often during dose escalation. Severe intolerance at the lowest dose (0.25 mg) is unusual.

The hallmark features of this case were:

- **Marked intolerance despite low-dose therapy**
- **Rapid weight loss in a normal-BMI individual**
- **Diarrhea and esophageal symptoms suggesting severe dysmotility**
- **Ultrasound-detected hepatic granulomas** that resolved after drug discontinuation

To our knowledge, hepatic granulomas with semaglutide have not been reported in detail, though hepatotoxicity has been described^{3, 4}. Granulomatous liver disease is most often associated with infections, autoimmune disorders, or drug hypersensitivity⁵. The temporal association, exclusion of other causes, and resolution after drug cessation suggest a semaglutide-induced drug-hypersensitivity reaction. However, a transient immune dysregulation is possible.

Consent

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

This case highlights the importance of considering drug-induced hepatic granulomas in patients presenting with unexplained hepatic abnormalities while on semaglutide. Clinicians should also exercise caution in prescribing semaglutide to individuals with low baseline BMI, where even modest weight loss may result in underweight status.

Conclusion:

This case underscores a rare but clinically significant adverse effect of low-dose semaglutide: severe gastrointestinal intolerance and hepatic granulomas. Clinicians should maintain vigilance for atypical presentations, particularly in patients with low BMI. Early recognition and discontinuation of semaglutide can lead to complete recovery and may prevent unnecessary invasive procedures.

Patient Perspective

The patient expressed distress at the severity of her gastrointestinal symptoms and the rapid weight loss. Although initially motivated by the weight reduction benefits of semaglutide, she now prefers lifestyle-based strategies for weight management and is cautious about future pharmacologic interventions.



Conflicts of Interest

The authors declare no conflicts of interest.

Funding

No funding was received for this study.

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