

## GLP-1 receptor agonist-associated eosinophilic duodenitis presenting as a bowel obstruction : a case report and literature review

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### Abstract

**We report a rare drugs adverse effect of a GLP1-RA, presenting as severe gastric stasis, eosinophilic duodenitis, and high bowel obstruction. The patient, treated with oral semaglutide for type 2 diabetes and obesity, developed progressive upper gastrointestinal symptoms culminating in faecal vomiting. Endoscopic and histological findings revealed marked eosinophilic infiltration of the duodenum. To our knowledge, this is the first reported case linking semaglutide to eosinophil-driven duodenitis causing mechanical obstruction. As the use of GLP1-RAs expands, clinicians should be aware of rare but potentially serious gastrointestinal adverse effects, particularly in patients with risk factors for impaired motility. Early recognition of symptoms and consideration of underlying eosinophilic gastrointestinal disease are essential for timely diagnosis and management. (Acta gastroenterol belg., 2026, 89, 93-96).**

### Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are a widely used class of medications approved for the management of type 2 diabetes mellitus and obesity. Their glucose-lowering effect is mediated by enhanced glucose-dependent insulin secretion, delayed gastric emptying, and appetite suppression. Among their therapeutic benefits, weight loss is particularly significant, making them an appealing option in patients with both metabolic conditions (1). This drug class includes agents such as lixisenatide, exenatide, dulaglutide, liraglutide, and semaglutide. Semaglutide, a long-acting GLP-1RA, is available in both subcutaneous and oral formulations and has shown superior efficacy in glycemic control and weight reduction compared to earlier molecules (1,2). Despite their favorable metabolic profile, GLP-1RAs are associated with gastrointestinal adverse effects, the most common being nausea, vomiting, and diarrhea—generally mild and self-limiting (2,3). However, emerging data point to a spectrum of more severe and underrecognized complications, including acute pancreatitis, gastroparesis, and intestinal obstruction. A recent meta-analysis suggests that GLP-1RAs may increase the risk of intestinal obstruction by up to 4.5-fold (4).

Among all the GLP-1RAs, cases of bowel obstruction are less common with semaglutide. It was only in late 2023, that the Food and Drug Administration (FDA) reported the first 33 cases of ileus linked to semaglutide (5) In addition, only 20 cases of eosinophil-related

diseases associated with GLP-1RAs have been reported in the literature (6).

In this article, we present the case of a patient who developed upper intestinal obstruction associated with eosinophilic duodenitis following the initiation of semaglutide. To our knowledge, no cases of GLP-1RA induced eosinophilic enteritis have been previously reported.

### Case report

A 58-year-old man presented to the emergency department with a recent onset of upper gastrointestinal symptoms that had progressed over the course of one week. He initially reported nausea, foul-smelling belching, and abdominal bloating—nonspecific symptoms that are commonly encountered in outpatient settings. However, over the two days preceding admission, his condition worsened with complete absence of flatus and bowel movements, culminating in episodes of feculent vomiting—findings consistent with high-grade proximal intestinal obstruction.

His medical history was notable for type 2 diabetes mellitus (treated for more than 8 years), morbid obesity (BMI at 35,4 kg/m<sup>2</sup>), obstructive sleep apnea, and a prior ischemic stroke. Chronic medications included aspirin (80 mg daily), bisoprolol (2.5 mg daily), ezetimibe (10 mg daily), metformin (850 mg twice daily), and atorvastatin (20 mg daily). Oral semaglutide had been initiated three months earlier and titrated to its maximum dose (14 mg per day) four days before presentation.

On examination, the patient was afebrile and hemodynamically stable. The abdomen was markedly distended and tympanic, with absent bowel sounds. Cardiac, pulmonary, and neurological examinations were unremarkable.

Laboratory studies showed hemoconcentration (hemoglobin 17.8 g/dL, normal value 13.3–16.7 g/dL),

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normal white blood cell count (7,600/mm<sup>3</sup>, normal value 4,000–10,000/mm<sup>3</sup>), C-reactive protein 3 mg/L (normal value ≤ 5 mg/L), and elevated lactate dehydrogenase (LDH) level of 268 U/L (normal value ≤ 250 U/L). Renal function and serum electrolyte levels were within normal limits.

An abdominal CT scan showed significant distension of the stomach (Figure 1), with no clearly visible obstruction and no dilatation of the small bowel or colon. However, a transitional zone was noted at the junction between the second and third portions of the duodenum. A nasogastric tube was placed and over a litre of blackish, faecal fluid was drained.

After admission to the gastroenterology department, an upper gastrointestinal endoscopy was performed. The gastroscopy revealed a diffuse erythematous gastropathy and multiple linear ulcers in the body of the stomach, likely exacerbated by significant gastric distension. The duodenal mucosa appeared normal and there was no evidence of obstruction (Figure 1). Gastric and duodenal biopsies were performed. Histological analysis revealed chronic active gastritis involving both the fundic and antral mucosa, and immunohistochemical testing for *Helicobacter pylori* was negative. However, subacute duodenitis with significant eosinophilic infiltration was observed in the duodenal biopsies (Figure 2). Notably, the patient had never presented with peripheral blood eosinophilia.

Additional tests were performed to further investigate eosinophilic duodenitis, including serologies for parasites (*Toxocara*, *Fasciola*, *Echinococcus granulosus*, and *Trichinella*), tryptase levels, total IgE, lymphocyte immunophenotyping, antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), and three stool examinations for parasites. All results were negative. Serology for celiac disease was also negative.

Semaglutide was discontinued on admission, leading to a rapid improvement in the patient's condition. PPIs were initiated (pantoprazole 40 mg once daily) in the context of gastric ulceration. The nasogastric

tube was successfully removed after 48 hours, and bowel function returned to normal shortly thereafter. The patient was subsequently discharged after a 7-day hospitalization. A follow-up gastroscopy performed 8 weeks after semaglutide discontinuation showed resolution of the gastric ulcers, but persistent food stasis was noted, which is likely indicating underlying diabetic gastroparesis. Control biopsies showed complete resolution of eosinophilic infiltration in the duodenum. This histological improvement after discontinuation of semaglutide supports the hypothesis of a drug-induced cause.

## Discussion

Eosinophilic gastroenteritis, first described in 1937, is a rare condition characterised by the infiltration of eosinophilic granulocytes into the intestinal wall (7). This condition is more commonly observed in the paediatric population, but can also affect adults, particularly those between the ages of 40 and 50 years (7-10). There is a higher prevalence in women and in the Caucasian population (9). The exact pathophysiology of eosinophilic gastroenteritis remains unclear, but it is thought to result from an abnormal allergic response to an allergen (7,12).

The most common symptoms are abdominal pain, nausea, vomiting, diarrhea, and even constipation. These may also be complicated by exudative enteropathy, steatorrhea, and, ultimately, upper or lower gastrointestinal obstruction (7). The differential diagnosis for eosinophilic infiltration of the intestinal wall includes parasitic infections (such as *Strongyloides*, *Trichinella*, *Toxocara*, *Ascaris* spp.), celiac disease, vasculitis, drugs, connective tissue disorders, inflammatory bowel diseases, lymphoma, and hyper-eosinophilic syndrome (7,8).

Surprisingly, drug-induced eosinophilic gastroenteritis is extremely rare, with only a few drugs, such as tacrolimus, clozapine, carbamazepine, and NSAIDs

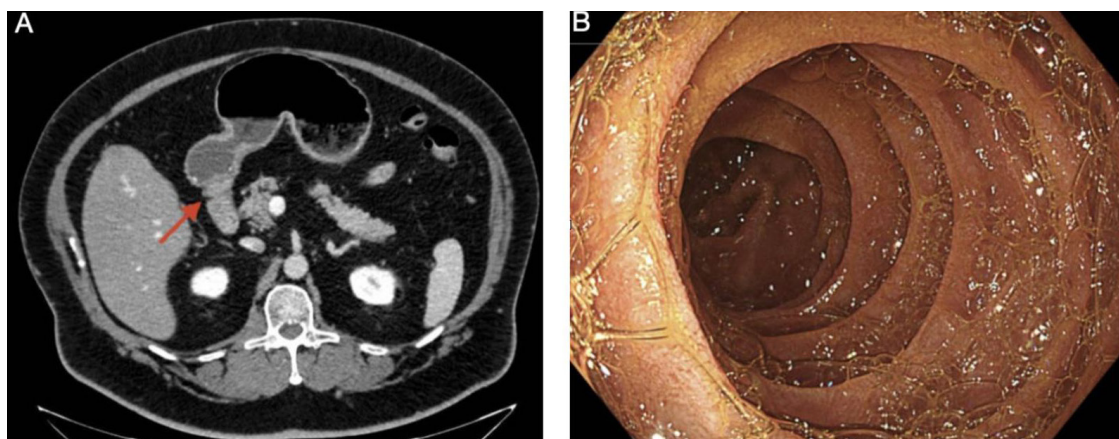


Figure 1. — (A) Abdominal CT scan showing gastric distension with transitional zone between the second and the third parts of the duodenum.

(B) Upper gastrointestinal endoscopy showing a normal duodenal mucosa without obstruction.

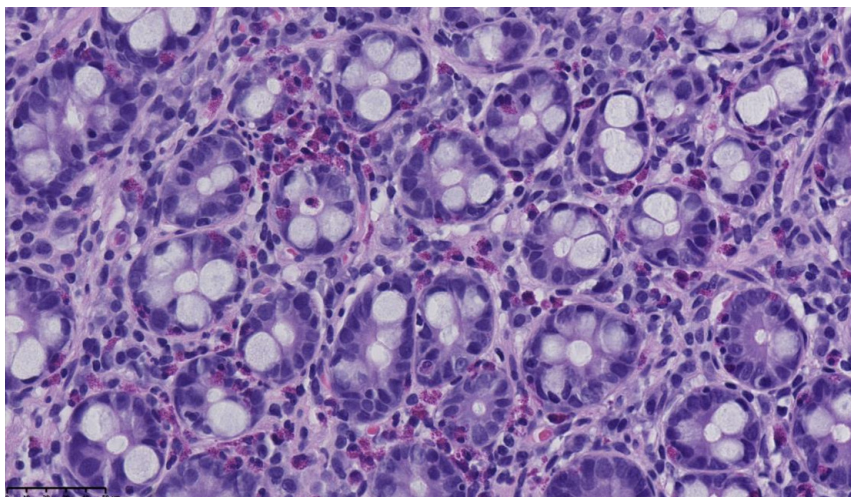


Figure 2. — Duodenal biopsies. Presence of an excess of eosinophilic polymorphonuclear cells clustered between the duodenal glands.

(non-steroidal anti-inflammatory drugs), having been implicated in the literature (11).

Recently, there have been reports of eosinophil-related disorders with GLP-1RAs. In 2023, an article documented 21 cases of hypereosinophilic syndrome associated with GLP-1RAs (4). The reported manifestations included blood eosinophilia, rash, hepatitis, bullous pemphigoid, nephritis, panniculitis, eosinophilic pneumonia, and eosinophilic fasciitis (4,6). While the pathophysiology underlying these eosinophil-related disorders is not yet fully understood, there is evidence that eosinophils express GLP-1 receptors, which appear to have a modulatory effect. Exposure to GLP-1RAs has been shown to reduce the expression of surface activation markers on eosinophils following lipopolysaccharide (LPS) stimulation and to decrease eosinophil production of interleukins, such as IL-4, IL-8, and IL-13, but not IL-5 (7). This cytokine perturbation results in a paradoxical effect responsible for the activation of eosinophils.

In addition, GLP-1RAs have been associated with an increased risk of gastrointestinal obstruction (1,4,13). An analysis of the WHO pharmacovigilance database (Vigibase) showed a 4.5-fold increased risk of gastrointestinal obstruction (ROR 4.52, 95% CI: 3.87–5.28) (4). Similar findings were reported in a study of 25,617 users of GLP 1RAs (13). The risk of obstruction appears to increase with the duration of treatment, becoming significant after 1.6 to 1.8 years of use (1,13). Although the exact mechanisms are not yet fully elucidated, GLP-1RAs are thought to reduce intestinal motility, possibly through their effects on presynaptic receptors that modulate the release of nitric oxide (NO) within the enteric nervous system (13). This risk is further exacerbated in patients with diabetes, who may already have impaired intestinal motility due to diabetic neuropathy (4,13). However, we have not found any physiopathological mechanisms or reported cases in the literature suggesting an eosinophilic infiltration of the intestinal wall associated with GLP-1RAs.

In our patient, given the lack of other identifiable causes and the recent initiation of semaglutide, we hypothesise that the bowel obstruction was exacerbated by semaglutide in the setting of pre-existing diabetes-related intestinal motility disorders. The presence of eosinophilic infiltration in the duodenum supports a drug-induced aetiology for the intestinal obstruction, consistent with eosinophilic enteritis as part of an eosinophil-related disorder associated with GLP-1RAs. To our knowledge, this is the first reported case of such an association in the literature.

However, we cannot exclude that the introduction of proton pump inhibitors (PPIs), given in the context of gastric ulceration, may have contributed to the clinical improvement.

With the expanding use of GLP-1 receptor agonists, clinicians should remain vigilant for rare but potentially severe gastrointestinal adverse effects. The onset of non-specific upper gastrointestinal symptoms warrants early diagnostic evaluation. As illustrated in this case, rapid clinical deterioration underscores the necessity of prompt discontinuation of the drug when unexplained decompensation occurs.

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