A Slim Price to Pay? A Rare Esophageal Complication of Tirzepatide

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Abstract- A 42-year-old male with no significant comorbidities presented with hematemesis and a transient loss of consciousness. He had recently initiated pharmacologic therapy for weight loss and was on the fourth dose at the time of presentation. Upper gastrointestinal endoscopy revealed a Mallory-Weiss tear as the source of bleeding. While such tears are classically associated with forceful vomiting or retching, the temporal relationship between symptom onset and initiation of weight-loss therapy raises consideration of contributing factors. This case underscores the need for clinical awareness of gastrointestinal mucosal injury in patients receiving newer anti-obesity medications and highlights the importance of early recognition and supportive management in preventing complications.

Keywords- Weight loss, syncope, obesity, GLP-1 receptor agonists, gastroparesis, hematemesis, Mallory weis tear.

1.INTRODUCTION

Mallory-Weiss tear (MWT) is a longitudinal mucosal laceration at the gastro esophageal junction, often resulting in upper gastrointestinal (GI) bleeding. It typically arises secondary to a sudden increase in intra-abdominal pressure, most commonly due to forceful retching or vomiting. MWT accounts for approximately 5%–10% of non-variceal upper GI bleeding episodes and, in most cases, resolves spontaneously. However, significant hemorrhage requiring endoscopic or supportive management may occur.

Tirzepatide, a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has demonstrated substantial efficacy in the management of type 2 diabetes mellitus and obesity. Despite its therapeutic benefits, gastrointestinal adverse effects such as nausea, vomiting, and abdominal discomfort are frequently observed, particularly during dose escalation.

We present a rare case of hematemesis secondary to a Mallory-Weiss tear that developed shortly after administration of tirzepatide. This case highlights a potentially serious gastrointestinal complication associated with the emetogenic effects of GLP-1 receptor agonists and emphasizes the importance of close clinical monitoring during initiation and dose titration of these agents.

2. LITERATURE REVIEW

Several studies have documented nausea, vomiting, diarrhea, and dyspepsia as the most frequent side effects of tirzepatide, with dose-dependence noted in clinical trials

In addition to these well-recognized effects, pancreatitis, gastroesophageal reflux disease (GERD), and drug-induced liver injury (DILI) have also been reported in isolated cases, particularly among those with pre-existing GI or hepatic conditions

The occurrence of a Mallory-Weiss tear as a direct consequence of its emetic effects is a new finding. This report highlights the importance of recognizing and managing severe vomiting as a potential risk factor for upper gastrointestinal bleeding in patients using tirzepatide, particularly during the initial treatment phase or dose escalation

3.METHODOLOGY

A 42-year-old male with a history of prediabetes (hba1c 5.8%) presented to the emergency department (ed) with complaints of loose stools for the past 48 hours, followed by vomiting for 24 hours, and

hematemesis for the past 60 minutes. The patient also reported experiencing two episodes of syncope prior to arrival.

Upon initial assessment, the patient was hemodynamically stable, with vital signs within normal limits, and a glasgow coma scale (gcs) score of 15. His CNS examination was normal. There were no signs of neurological deficits or altered mental status.

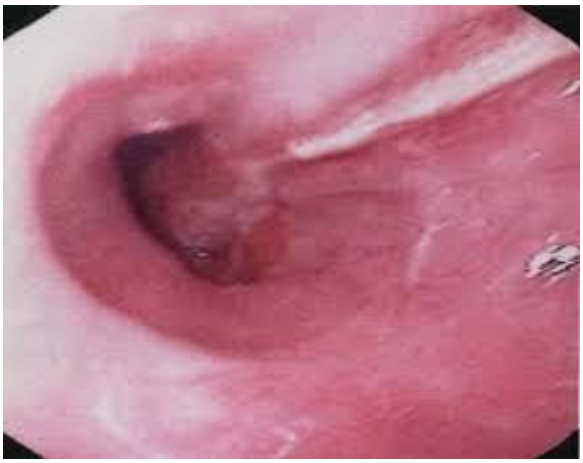
The patient was noted to have syncope prior to arrival, which was attributed to dehydration secondary to ongoing vomiting and diarrhea. An ecg was performed, which revealed normal sinus rhythm without evidence of ischemia or arrhythmia. Neurologist opinion was taken. CT brain was done and was normal.

Laboratory findings revealed a hemoglobin level of 12.9 g/dl, and liver function tests (lfts) were normal, excluding acute liver pathology. The patient's electrolyte panel was unremarkable. Given the clinical presentation of hematemesis and vomiting, an upper gastrointestinal (ugi) endoscopy was performed, which revealed clotted blood at the gastroesophageal junction and a longitudinal tear, confirming the diagnosis of mallory-weiss tear.

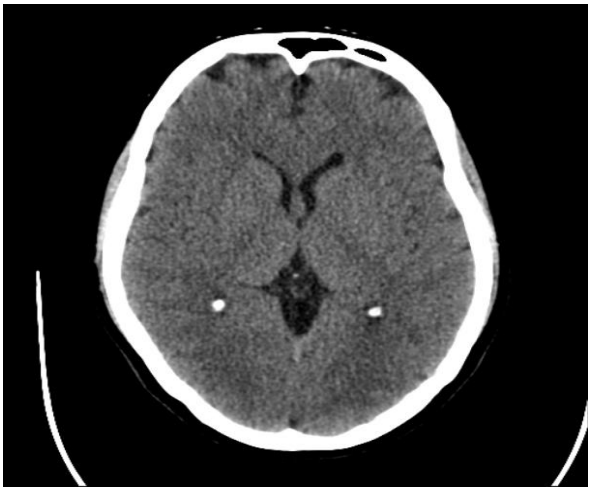
Management and Outcome

The patient was initiated on intravenous proton pump inhibitor (PPI) infusion to reduce gastric acid secretion and facilitate mucosal healing. His vomiting subsided within hours, and there was no evidence of recurrent bleeding. He was closely monitored for signs of hemodynamic instability, but he remained stable throughout his hospital stay.

Over the course of a 3-day hospitalization, the patient’s condition improved, and his symptoms resolved. He was discharged with appropriate instructions for follow-up care, including hydration, dietary adjustments, and prediabetes management. The patient was advised to avoid potential risk factors for further vomiting, such as alcohol and stress, and to follow up with his primary care provider for ongoing care and monitoring.



UGI SCOPY SHOWING MALLORY WEIS TEAR



CT BRAIN PLAIN

4.DISCUSSION

The hematemesis observed in this patient can be attributed to a mallory-weiss tear, which was precipitated by recurrent vomiting associated with gastroparesis. Gastroparesis, a condition involving delayed gastric emptying, is a well-known complication of certain medications, particularly those that affect gastric motility, such as tirzepatide. While tirzepatide is known to cause gastrointestinal side effects such as nausea, vomiting, and indigestion, the direct association with gastroparesis and its contribution to mallory-weiss tear has not been previously reported in the literature.

The underlying pathophysiology can be understood through a combination of mechanisms. Tirzepatide, a dual glp-1 and gip receptor agonist, slows gastric

emptying as part of its pharmacodynamic action. This gastric stasis predisposes patients to nausea, vomiting, and gastroesophageal reflux disease (gerd). The delayed gastric emptying leads to prolonged distention of the stomach, which, when coupled with recurrent vomiting, increases the risk of retching and increased intra-abdominal pressure.

In this patient, the forceful vomiting—exacerbated by the gastroparesis induced by tirzepatide—caused retching at the gastroesophageal junction, leading to the longitudinal mucosal lacerations that characterize a Mallory-Weiss tear. These tears result in upper gastrointestinal bleeding, manifesting as hematemesis, as seen in this case. The repetitive vomiting and retching cycle, compounded by delayed gastric emptying, created an environment conducive to the development of the tear.

This case is particularly notable because the connection between tirzepatide-induced gastroparesis and the occurrence of Mallory-Weiss tear has not been documented in the current literature. Although gastrointestinal adverse effects like nausea and vomiting are well-recognized, the mechanical stress from gastroparesis, causing upper GI bleeding, is a previously unreported consequence. This highlights the need for increased awareness of the potential for gastric motility disorders induced by tirzepatide and their impact on the gastrointestinal tract, especially in patients who experience severe vomiting.

In conclusion, this case underscores the unrecognized risk of Mallory-Weiss tear associated with the use of tirzepatide, a medication that affects gastric motility. It is crucial for clinicians to be aware of the possibility that medications known to slow gastric emptying can lead to gastroparesis, vomiting, and ultimately, upper gastrointestinal bleeding. This novel association warrants further investigation to better understand the long-term and potentially severe gastrointestinal side effects of tirzepatide in clinical practice.

This version provides a deeper dive into the mechanism behind the Mallory-Weiss tear, emphasizing that the tirzepatide-induced gastroparesis and its contribution to the hematemesis and upper GI bleeding has not been previously described in the literature.

5.CONCLUSION

This case poignantly underscores the unforeseen consequences of tirzepatide-induced gastroparesis, a condition that led to recurrent vomiting, retching, and ultimately a Mallory-Weiss tear resulting in hematemesis. While prediabetes is often manageable with lifestyle modifications like regular exercise and dietary changes, this patient, despite having a relatively controlled HbA1c, found himself vulnerable to an unexpected and serious gastrointestinal complication. The gastroparesis induced by tirzepatide went unrecognized, creating a cascade of events that led to the upper GI bleeding.

This case highlights the importance of holistic care, where medication side effects must be weighed against underlying metabolic conditions. The impact of prediabetes and a lack of preventive measures like exercise cannot be understated, yet this patient's experience reveals a new clinical dimension—the potential for medication-induced gastrointestinal complications. It serves as a reminder of the necessity for vigilant monitoring of patients on medications with gastric motility effects and the need to consider all aspects of a patient's health to prevent such serious outcomes.

Future studies should focus on the impact of GLP-1 receptor agonists on gastric motility, vomiting, and upper GI bleeding. Understanding these medication-induced complications will be crucial in identifying high-risk patients and developing preventive strategies. Additionally, personalized treatment plans that consider both metabolic health and medication side effects could improve patient outcomes and safety.

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