Response to reviewers: Thank you very much for taking the time to review this case report. We have responded to each comment separately below.

Reviewer #1: The authors reported a rare case of diabetic ketoacidosis complicated with acute esophageal necrosis. The report is well-written and nicely presented. I have only some minor comments.

1. Please provide information on the age and sex of the patient in the abstract.
The patient was a 63 year old caucasian male.

2. Did the patient have alcohol abuse?
The patient did not have a significant alcohol intake history.

3. Please provide information on the body weight and length or body mass index of the patient.
The patient was 94kg, 1.778m tall, with a body mass index of 31.14 kg/m².

Reviewer #2: Comments to the author This report describes a rare but serious complication of diabetic ketoacidosis. However, certain issues need to be addressed.

1. Title- I would suggest to remove the words " case report" and rephrase the title
My understanding is that the word case report must be in the title as per the care checklist but the title has been reframed as follows:
Acute esophageal necrosis as a complication of diabetic ketoacidosis: a case report

2. Abstract- "...newly started ketogenic diet"- Can physiological ketosis trigger the onset of DKA?
The patient with type 2 diabetes mellitus had recently started a ketogenic diet and this change in diet to restrict carbohydrate intake along with typical DKA triggers including poor glucose control and dehydration may have had additive effects leading to the patient developing DKA. A ketogenic diet alone is not a typical cause of DKA however there are case reports of ketogenic diets leading to ketoacidosis in both diabetic and non-diabetic patients.

How GLP-1 RA treatment can be associated with AEN?
DKA is a potential trigger for AEN based on previous case reports. GLP-1 RA may have potentiated DKA, and thus potentiated AEN indirectly. GLP-1 RA may have potentiated DKA, especially in combination with the new diet, because the GLP-1 RA increases ketogenesis and lipolysis. Furthermore, GLP-1 RA may have had a direct role in potentiating AEN as AEN can be caused by corrosive injuries and the gastroparesis and resulting increased gastric reflux associated with GLP-1 RA may have contributed to the development of AEN.

Please provide expansion for EGD
Expansion is as follows:
Esophagogastroduodenoscopy (EGD) was performed, which showed severe class D esophagitis involving the entire esophagus. There were circumferential black, necrotic inflammatory changes in the mid to distal esophagus that stopped abruptly at the GEJ thought to represent AEN which can be seen in Figure 1. Biopsies were not taken of the necrotic tissue. Erosions were seen in the body and antrum of the stomach, and multiple clean based ulcers were seen in the duodenum. Biopsies were taken of the gastric and duodenal mucosa, and histology report showed chronic gastroduodenitis with no sign of H. pylori or infectious organisms as well as no evidence of neoplasia.

3. Case Report- "non-insulin dependent diabetes mellitus" should be replaced with Type 2 diabetes mellitus

This will be corrected in the case report revisions.

Duration of diabetes is not mentioned- This is important in this case scenario "he was switched from liraglutide to semaglutide"- Did the patient tolerate liraglutide well?

The patient had diabetes for several years initially maintained with metformin. The liraglutide was added for one year to aid with weight loss but was ineffective, though it was well tolerated. The primary care physician switched the patient from liraglutide to semaglutide and one week following the first dose presented with DKA.

Body weight data missing, BP data missing

The patient was 94kg, 1.778m tall, with a body mass index of 31.14 kg/m². His blood pressure on presentation was 136/81 though he was taking ramipril 5mg daily for hypertension.

Please provide the blood glucose level at admission

On initial presentation his blood glucose was 17 and peaked at 82mmol/L (4-7mmol/L).

Please provide the reference range for B-hydroxybutyrate

His B-hydroxybutyrate level was 10.20mmol/L and the reference range is <0.25mmol/L

Missing citation of figure 1

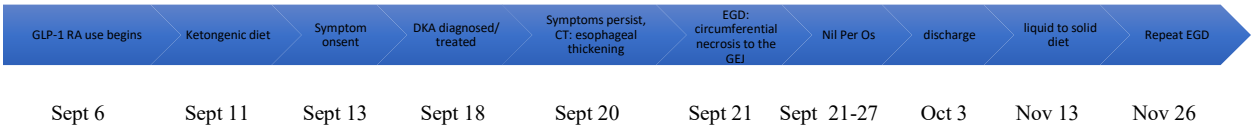

Figure 1:
Timeline of illness from symptom onset to resolution of esophageal damage in 63 year old caucasian man with diabetic ketoacidosis and acute esophageal necrosis.

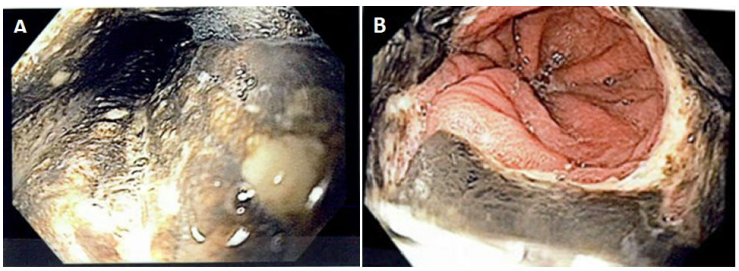

Figure 2:

Endoscopic image of the presented patient's mid-distal esophagus with circumferential black discoloration of the mucosa likely to be necrotic tissue (A). Distal esophagus with circumferential black discoloration of the mucosa with clear demarcation at the gastroesophageal junction in keeping with acute esophageal necrosis (B).

"sucralfate and PPI twice daily"-Any advantage of concomitant use?

The dual use of sucralfate, a coating agent, and a PPI to inhibit further gastric acid secretion, are both agents that improve symptomatology and severity of esophagitis. The concomitant use of both is a local practice in Hamilton Ontario for short term use in severe esophagitis.

What treatment regimen for glycemic control was advised at discharge?

At discharge metformin and GLP-1 RA were discontinued and insulin aspart 5 units three times daily and insulin glargine 15 units nightly.

4. Discussion- Author may provide the details of previous cases in tabular format Ketogenic diet may act as a trigger. Contrasting nutritional ketosis with ketoacidosis, DKA results from absolute insulin deficiency (Ref. 12- misdiagnosis of LADA). Was this patient insulin deficient?

Previous case reports have discussed a case of ketoacidosis due to ketogenic diets in a patient with type 2 diabetes and LADA respectively. I am unclear what is meant by the first portion of this comment, if further actions are required, please clarify. It can be concluded that the patient in this case report was correctly diagnosed with type two diabetes after a work up for LADA, including c-peptide levels were completed and were within normal range. The patient's c-peptide was 1087picomol/L (reference range 370-1470picomol/L)

No data on microvascular complications in case report section In a patient with diabetes mellitus.....making them more prone to ketoacidosis- Ketosis prone T2DM is common in people with certain ethnic background- is it relevant in your case?

The patient did not have any known/significant microvascular complications.
The patient was a caucasian male which is not believed to be an especially prone ethnic group.

Patient was switched over to weekly semaglutide- It appears from the timeline that patient received only one injection before symptom onset

The liraglutide was added for one year to aid with weight loss but was ineffective, though it was well tolerated. The primary care physician switched the patient from liraglutide to semaglutide and one week following the first dose presented with DKA.

second revision comments to be addressed:

Reviewer #1: The revised manuscript is more polished. Authors have addressed all the queries raised during initial review appropriately. Further comments to the author:

Introduction- Please check the reference order. Ref. 10 cited before Ref 5-9

Thank you, this will be corrected.

Replace "type two" with "type 2" throughout the manuscript

Thank you, this will be corrected.

Please provide citation for Figure 1 in the text.

This has been corrected in the HPI section as follows: When the pain and nausea peaked 5 days following symptom onset, see figure 1 for timeline, he presented to the hospital.

Case Presentation- His glucose was initially.....peaked at 82 mmol/L. Is that a lab value or POC reading?

82mmol/L was a lab value not a POC reading.

Final Diagnosis- It is not clear why authors wanted to rule out LADA in a 63 year old non-insulin requiring patient with h/o diabetes for several years. Moreover autoantibodies (e.g GAD65) were not performed.

As ketoacidosis in patients with T2DM who are not insulin deficient is uncommon, C-peptides were ordered to determine insulin deficiency as well as to rule out the possibility of LADA causing DKA. As his c-peptide levels were normal, further workup of LADA was not pursued.

Discussion- Authors may provide the data of previously reported cases in a tabular format for better impression of this clinical vignette. Ketoacidosis is uncommon in a patient with T2DM who is not insulin deficient (normal C-peptide).

Thank you for the feedback, we have included a brief summary table as table 1.

No definite trigger was identified for ketoacidosis.

The likely trigger, though this cannot be confirmed, for ketoacidosis was the ketogenic diet in combination with dehydration from the manual labour followed by several days of anorexia that preceded presentation.

Cases of DKA reported in association with GLP-1RAs particularly after rapid reduction or discontinuation of concomitant insulin. Therefore, not a concern specific to treatment with GLP-1RAs. Authors need to clarify this issue.

Unclear about the intent of the reviewer comment, however clarified in the case is the role of GLP-RA1s that lead to gastroparesis and therefore render the esophagus more prone to AEN.

At what levels of glycemia the C-peptide was checked? Please confirm whether it is a fasting or post-meal value?

It was done fasted at 8 hours nil per os.