Peer Review File

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Round 1

Comment 1: I think it is inappropriate to use the term Boerhaave's syndrome when there is an underlying lesion in the esophagus such as Zollinger-Ellison syndrome. This is because the cause of Boerhaave's syndrome is idiopathic and is defined as having no underlying esophageal lesion. I think the term esophageal perforation should be used instead of the term Boerhaave's syndrome.
Reply 1: The authors appreciate that they may have incorrectly applied the term Boerhaave's syndrome to the cases described in the report and agree with the reviewer that this should be changed to reflect the presence of underlying esophageal pathology in these patients.
Changes in the text: The term Boerhaave's syndrome has been changed throughout the text to "esophageal perforation". This term has been changed in the abstract (lines 23 & 31); removed from the key-words; changed in the key-findings (line 63, 70 & 73); introduction (line 98 & 104); discussion (line 258, 270); and conclusion (line 409).

Round 2

Comment 1. Please add "case report" to Key-Words and considering keywords no more than 5, authors can preserve one among esophageal perforation and Boerhaave's syndrome.
Reply 1: Thank you for this suggestion.
Changes in the text: We have removed "Boerhaave's syndrome" from the key-words and replaced it with "case report" (line 38).

Comment 2. Line 20, before pointing out " Esophageal perforation in the setting of Zollinger-Ellison syndrome (ZES) is rare and requires timely management for successful treatment", authors should give a concise introduction about Zollinger-Ellison syndrome, such as epidemiology and clinical presentation. And then, explicitly state the unique point of this case report in such background.
Reply 2: We agree that further background information can be provided for ZES, though what makes the two cases described unique, is that these patients presented with esophageal perforation. For this reason, and due to word-limit restrictions, we have kept the background information concise.
Changes in the text: We have elaborated on the etiology and presenting symptoms of ZES in the abstract (lines 20-22).

Comment 3. Lines 22-32, considering that many readers may first read the Abstract and then decide whether to read the full text. Therefore, the case description in the

Abstract is important and some details need to report. Taking case 1 as an example, authors are advised to state patients' demographic characteristics (e.g., age and sex), main symptoms (e.g., nausea, vomiting, abdominal pain), past medical history (e.g., suspected ZES, severe esophagitis, gastritis and duodenitis with recurrent gastrointestinal bleeds, and chronic abdominal pain), important clinical findings (e.g., perforation of the distal esophagus at the gastroesophageal junction), and the interventions also including right thoracotomy, decortication. The same applies to case 2, but additional outcomes and follow-up (if applicable) are needed.
Reply 3: We agree that further demographic information, presenting symptoms, and past medical history, would be helpful to provide to readers in the abstract.
Changes in the text: Additions to the case descriptions have been provided in the abstract (lines 29-33, and 36-38).

Comment 4. In the introduction, it's suggested to explain what ZES is and its common clinical presentation and then mention "Esophageal perforation is a rare complication of Zollinger-Ellison syndrome (ZES)". Furthermore, the relationship of the three - ZES, gastrinoma, and multiple endocrine neoplasia type 1 - needs to be clearly reported. For authors' reference, ZES is caused by the secretion of gastrin from neuroendocrine tumors of the duodenum or pancreas; 20-30% of gastrinomas are associated with multiple endocrine neoplasia type 1 (It's just an example which comes from UPToDate).
Reply 4: The authors agree additional background information would benefit readers.
Changes in the text: In the introduction, we have elaborated on the etiology of ZES and its signs/symptoms (lines 78-88).

Comment 5. The authors need to clarify in the Introduction whether any cases of ZES with Boerhaave's syndrome have been reported in previous literature. If have, the authors should compare those studies in the Introduction and highlight the unique points of this case report. For example, is this the first case report of ZES with Boerhaave's syndrome and postoperative aorto-gastric fistula?
Reply 5: There has been one case report on Boerhaave's syndrome in a patient with ZES though, as the Reviewer identified as a major concern for this report, this may not be the appropriate terminology to apply, as Boerhaave's syndrome is idiopathic. Nevertheless, we have referenced cases in which esophageal perforation occurred in patients with ZES.
Changes in the text: See the introduction (lines 92-102).

Comment 6. Line 69, it's great for authors to specify this patient's past medical history, how about family history? Is there a peptic ulcer disease family history or a family history of MEN1? The same applies to case 2.
Reply 6: Thank you for identifying where there may have been a lack of information.
Changes in the text: We have specified the patients' relevant family history in lines 124-125, and 195-196.

Comment 7. Some important time points need to give specific dates, such as symptom onset, presentation, transfer, progress, improvement, re-hospitalization, follow-up, and death time. Please avoid reporting "xx days later" or "POD xx".
Reply 7: We agree specific dates are more meaningful to the reader, however our institution is the sole provider of thoracic surgery services for approximately 1.2 million patients. We feel providing the exact dates introduces a reasonable risk of the patients being identified compromising patient confidentially. At present we have left the timeline as POD XX but remain open to suggestions from the editors on how we can ensure that we are protecting the identity of our patients.
Changes in the text: None, but we remain open to suggestions.

Comment 8. Line 93, "…started on broad spectrum antibiotic and antifungal therapy, as well as total parenteral nutrition (TPN)", please specify the detailed therapeutic intervention information of two cases, such as specific types of antibiotics, dosage, frequency, and duration.
Reply 8: Further information can be provided.
Changes in the text: We have clarified the antimicrobial regimens for both patients (lines 149-150, and 214-215).

Comment 9. Line 162, "...the patient recovered well and was discharged home on POD 18", up to now, how about the patient outcome? It would be useful for authors to add follow-up outcomes, including important diagnostic and test results.
Reply 9: Additional information can be provided.
Changes in the text: The patient's follow-up course has been described through lines 241-246.

Comment 10. It's suggested to add a timeline. The timeline should present relevant events in the patient's history in chronological order in a figure or table, enabling the core elements of the case report to stand alone. Figures can be integrated into the timeline. Here is an example from our sister journal for your reference: https://tlcr.amegroups.com/article/view/35939/24197
Reply 10: A timeline may certainly provide clarity to readers regarding both patient's trajectories; however, we found this challenging and are open to suggestions/edits on the timelines we came up with.
Changes in the text: Figures 1 and 2 show the timelines for Case 1 and Case 2, respectively (see page 17). All previous figures have been removed.

Comment 11. We encourage authors to discuss the strengths and limitations of this case report.
Reply 11: The strengths and limitations can be included in the discussion.
Changes in the text: The strengths and limitations have been added (lines 265-272).

Comment 12. Line 209, " Consideration of stent placement at the time of initial repair

may have prevented the leak and the subsequent empyema, however, the second case highlights that esophageal stenting was not required to prevent a leak, though similar conditions were present". Would you elaborate analysis of this situation? We strongly hope authors can share their insights on the circumstances in which to consider stent placement.

Reply 12: Thank you for pointing out this deficiency in the manuscript. Comments have been added sharing our insight on stent placement at the time of the initial operation.

Changes in the text: **:** The following text has been added to lines 365-372. “Utilization of an esophageal stent at the time of the initial operation is a challenging surgical decision. Several factors should be considered by the operating surgeon: (1) the condition of the esophagus and stomach, (2) the degree of contamination in the local environment, (3) the patient’s acute metabolic status and (4) the patient’s past medical history. The surgeon must consider the risks of stent placement, including ischemia at the site of the repair secondary to the radial pressure from the stent and additional operating time to place the stent in an acutely ill patient, against the probability of the repair healing and the patient’s ability to tolerate a leak.”

Comment 13. Formatting

According to the author's instruction (https://cdn.amegroups.cn/static/public/2.5-Structure%20of%20Case%20Reports-template-V2022.11.4.docx?v=1677556343538)

1) Introduction should be restructured into three parts: a) Background, b) Rationale and knowledge gap, c) Objective.

2) Similarly, the discussion is structured in five parts: a) Key Findings, b) Strengths and limitations, c) Comparison with similar researches, d) Explanations of findings, e) Implications and actions needed.

Reply 13: The structure of the text has been changed to reflect the desired formatting.

Changes in the text: In the introduction, the background is provided in lines 78-91; the rationale and knowledge gap in lines 92-102; and objective in lines 104-114. The discussion includes key findings (lines 250-256), strengths and limitations (lines 265-272), comparison with similar studies (lines 282-313), explanation of findings (lines 314-364), and implications and actions needed (lines 365-386).