Author's response to reviews

Title: Colonic Ulcer Bleeding in the Setting of Invasive Aspergillus Infection in an Immunocompromised Patient

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Author's response to reviews: see over
1. Please include the study design in your title, i.e. Case report. For example: A presenting with B in C: a case report.

   Colonic Ulcer Bleeding in the Setting of Invasive Aspergillus Infection in an Immunocompromised Patient: A Case Report

2. Please include all the co-authors' email addresses in the Title page.

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3. Please reposition the Keywords section after the Abstract section.

   Keywords: Invasive Aspergillus, Aspergillosis, Gastrointestinal Bleeding, Immunosuppression

4. Please reposition the list of abbreviations used in the manuscript and their meanings after the Conclusions section.

   List of Abbreviations:
   IA: Invasive Aspergillus, ELISA: Enzyme-Linked Immunosorbent Assay, H&E: Hematoxylin and Eosin, GMS: Grocott's Methenamine Silver

5. Please restructure the Abstract section on page 2. The abstract must not exceed 350 words. Please do not use abbreviations or references in the abstract. The abstract should be structured into three sections and should make clear how the case report adds to the medical literature:

   a. Introduction - An introduction about why this case is important and needs to be reported. Please include information on whether this is the first report of this kind in the literature.

   b. Case presentation - Brief details of what the patient(s) presented with, including the patient's age, sex and ethnic background. If the Case reported is of multiple patients, please enumerate them accordingly.
Conclusion - A brief conclusion of what the reader should learn from the case report and what the clinical impact will be. Is it an original case report of interest to a particular clinical speciality of medicine or will it have a broader clinical impact across medicine? Please include information on how it will significantly advance our knowledge of a particular disease etiology or drug mechanism.

Abstract
Introduction
Invasive Aspergillus commonly involves the lungs, but can also affect other organs such as the skin, adrenal glands, central nervous system, liver, spleen and the gastrointestinal tract. Gastrointestinal aspergillosis is rare and is most often discovered in immunocompromised patients. There is only one other case report to our knowledge that describes the diagnosis being discovered on histopathological analysis of endoscopic biopsies of necrotic ulcers.

Case Presentation
A 36 year old Hispanic female presented with septic shock secondary to extensive Fournier gangrene and required multiple surgical debridement of the perineal and retroperitoneal area. Vital signs on admission were a temperature of 39.4ºC and blood pressure of 85/56mmHg, pulse rate of 108/min and respiratory rate of 25. Examination of the perineum/genital area revealed bilateral gluteal and perilabial edema, erythema and focal areas of necrotic tissue with purulent discharge. Other surgeries included small and large bowel resections with colostomy and diverting ileostomy. Eleven weeks after admission, the patient developed hematochezia from the colostomy associated with a decrease in hemoglobin and hematocrit to 6.4 g/dL and 20.2% respectively. Colonoscopy through the ostomy revealed blood throughout the colon and a 3 cm necrotic ulcer with an adherent clot in the transverse colon. Biopsies were taken from the edge of the ulcer. Histopathological analysis of the specimen with Grocott's methenamine silver stain revealed septated hyphae with the 45º angle branching that is morphologically consistent with Aspergillus species. The patient was treated with intravenous voriconazole for 30 days with a prolonged hospitalization but no recurrent bleeding.

Conclusion
Gastrointestinal aspergillosis is an unusual presentation of invasive Aspergillus associated with a high mortality rate. Characteristic features of gastrointestinal aspergillosis include invasion of the mesenteric arteries, intravascular thrombosis and subsequent tissue ischemia. Clinical manifestations of IA of the gastrointestinal tract can include fever, abdominal pain, ileus, peritonitis, bloody diarrhea or hematochezia. In an autopsy series of patients with invasive Aspergillus, 37 of 107 patients had aspergillus involvement of the gastrointestinal system; the most common pathological findings included ulcers and abscesses. Although rare, invasive aspergillosis may present with gastrointestinal bleeding associated with necrotic ulcers on endoscopic examination.

6. Please change the 'Case Report' section header to 'Case Presentation'.

Changed to Case Presentation

7. Please change the description of the patient’s gender to ‘male/female’.

Gender of patient was already described as female

8. Please include the Ethnicity of the patient in the Abstract and Case presentation sections.

Hispanic
9. Please include a Conclusions section as the last section of the text. This should state clearly the main conclusions of the research and give a clear explanation of their importance and relevance. Summary illustrations may be included.

Conclusions section was added to end of discussion section

10. Please include a Competing Interests section before the Reference list. If the authors have no competing interests, please state: "The authors declare that they have no competing interests."

Competing Interests:
The authors declare that they have no competing interests

11. Please include an Authors' Contributions section at the end of the manuscript, before the reference list. We suggest the following kind of format (please use initials to refer to each author's contribution):

“AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.”

Author Contributions:
JB participated in manuscript preparation and medical literature search.
CC participated in study design/planning, data interpretation, manuscript preparation/editing, medical literature search and analysis.
MZ participated in manuscript preparation/editing, literature search and analysis.
AT participated in histopathological examination/description and manuscript preparation.
AM participated in study design/planning, data interpretation, manuscript preparation/editing, literature search and analysis.

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Acknowledgements:
The authors have no acknowledgements.

13. Please upload the figures as separate files via the online submission system. They should not be included within the main manuscript document.

Figures on separate word document.