Gastrointestinal Bleeding in Patients with Severe SARS-CoV-2

Chiranjeevi Gadiparthi, MD, MPH[1], Abhilash Perisetti, MD[2], Hari Sayana, MD[3], Benjamin Tharian, MD, MRCP, FACP,FRACP[2], Sumant Inamdar, MD[2] and Andrew Korman, MD[1]

Gastrointestinal symptoms are common and frequently reported in Coronavirus Disease-2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is unclear if SARS-CoV-2 is associated with increased risk of gastrointestinal bleeding (GIB). Nevertheless, GIB in COVID-19 patients poses unique challenges to patients due to high-risk of concomitant respiratory failure and to endoscopy personnel due to risk of airborne transmission during endoscopic procedures. Many management issues related to COVID-19 are still being studied. In this case series, we attempt to discuss the important clinical implications related to the management of GIB in COVID-19 patients.

Am J Gastroenterol 2020;00:1–3. https://doi.org/10.14309/ajg.0000000000000719

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a respiratory-borne viral illness originated in December 2019, which became a pandemic with rapid spread across the globe (1). SARS-CoV-2 causes Coronavirus Disease 2019 (COVID-19) which is a clinical syndrome with a wide spectrum of involvement resulting in respiratory, gastrointestinal (GI), cardiac, and renal manifestations (2,3). Common GI symptoms include abdominal pain, nausea, vomiting, and diarrhea. GI bleeding (GIB) in patients with SARS-CoV-2 poses unique challenges, especially for endoscopists and other procedural staff because of the potential for aerosol spread. In this article, we report 3 hospitalized patients with SARS-CoV-2 infection with GIB and acute blood loss anemia with focus on management strategies.

CASE 1

A 53-year old white woman with history of Roux-en-Y gastric bypass (RYGB) surgery, hypertension, diabetes mellitus type 2 (T2DM), peripheral vascular disease and iron deficiency anemia was hospitalized for diabetic ketoacidosis and liver abscess secondary to complicated cholecystitis. The patient was managed with percutaneous drainage of the liver abscess by interventional radiology and extended intravenous antibiotic therapy for methicillin-resistant *Staphylococcus aureus* and was discharged to a subacute rehabilitation facility. Two weeks after discharge, she returned to the hospital with melena and acute blood loss anemia. She tested positive for SARS-CoV-2 by RT-PCR assay and developed acute hypoxic respiratory failure requiring supplemental oxygen of 15 L per minute via a nonrebreather mask. No history of nonsteroidal anti-inflammatory drugs (NSAIDs), anticoagulants, and antiplatelet agents use were noted. Rectal examination revealed melena. Hemoglobin measured in the emergency department was 5.9 g/dL, which dropped from the baseline level of 7.5 g/dL. The patient was transfused with 2 units of packed red blood cells (PRBCs) with appropriate improvement of hemoglobin to 7.5 g/dL. She was managed conservatively with periodic monitoring of blood counts and intravenous high-dose proton pump inhibitor (PPI) therapy. The patient responded without further episodes of GIB. However, she died on day 4 of hospitalization due to worsening hypoxic respiratory failure and she was not resuscitated as per her advanced directive and code status.

CASE 2

An 81-year-old Hispanic male patient with T2DM was admitted to the hospital with 2 episodes of rectal bleeding with clots and melena. The patient was previously hospitalized with urinary retention 1 week before this admission and had 2 episodes of rectal bleeding. He did not require blood transfusions or endoscopic intervention. His home medications do not include NSAIDs, anticoagulants, or antiplatelet agents. He did not require blood transfusions or undergo endoscopic procedures previously. The patient tested positive for COVID-19 based on RT-PCR. During previous hospitalization, the patient's hemoglobin dropped from 14.5 to 11.9 g/dL, which further dropped to 9.6 g/dL during the second hospitalization. Computerized tomography (CT) angiogram of the chest showed bilateral acute pulmonary emboli. He was started on intravenous heparin infusion. The patient received high-dose PPI and was managed conservatively with supportive care. On hospital day 5, the patient developed recurrent GIB with a large amount of melena and bright red blood per rectum with hemodynamic instability requiting intensive care unit (ICU) transfer. He received 2 units of PRBCs. CT angiogram was performed, which did not localize the bleeding vessel. The patient improved after conservative management and was discharged home on oral anticoagulation.

[1]Division of Gastroenterology, Hepatology and Clinical Nutrition, Saint Peter's University Hospital, New Brunswick, New Jersey, USA; [2]Division of Gastroenterology and Hepatology, University of Arkansas Medical Center, Little Rock, Arkansas, USA; [3]Division of Gastroenterology, University Texas Health Sciences Center, San Antonio, Texas, USA. **Correspondence:** Abhilash Perisetti, MD. E-mail: abhilash.perisetti@gmail.com.
Received April 21, 2020; accepted May 12, 2020; published online XXXX

Table 1. Patient demographics and clinical and laboratory parameters

	Patient 1	Patient 2	Patient 3
Age (y)	53	81	57
Gender	Female	Male	Female
Ethnicity	White	Hispanic	White
Home medications			
NSAIDS	No	No	No
Antiplatelets	No	No	No
Anticoagulants	No	No	No
GIB symptoms	Melena	Bright red/melena	Bright red per rectum
Oxygen saturation	99% on 15L NRB	98% on 2L NC	96% of RA
GBS score	11	7	3
Laboratory results			
Baseline Hb/Hct	7.8/24.8	11.9/36.7	10.5/34.1
Lowest Hb/Hct	5.6/17.4	6.6/20.8	6.7/23.8
PT/INR	1.32/15.4	1.2/13.9	1.1/12.4
Platelet count	373	323	290
BUN/Cr	31/2	22/0.9	10/0.8
D-dimer ng/mL	NA	1,654	3,076
Ferritin ng/mL	NA	463	376
LDH in U/L	NA	573	321
CRP mg/mL	162	160	197
No. of PRBCs	2 units	2 units	2 units
Chest x-ray	Bilateral infiltrates	Normal	Bilateral infiltrates
Outcome of GIB	Resolved	Recurrent GIB	Resolved

D-dimer, upper limit 211 ng/mL.
BUN, blood urea nitrogen; Cr, serum creatinine; CRP, C-reactive protein; GIB, gastrointestinal bleeding; GBS, Glasgow-Blatchford bleeding score; Hb, hemoglobin; Hct, hematocrit; INR, international normalized ratio; LDH, lactate dehydrogenase; NA, not available; NC, nasal canula; NRB, nonrebreather; NSAID, non-steroidal anti-inflammatory drug; PRBC, packed red blood cells; PT, prothrombin time; RA, room air.

CASE 3

A 57-year-old white woman with a medical history of hypertension and sick sinus syndrome with cardiac pacemaker presented to the hospital with flu-like symptoms for 7 days and high-grade fever for 4 days. The patient has no history of liver disease and does not take NSAIDs, anticoagulants, or antiplatelet agents. The patient tested positive for RT-PCR for COVID-19. She was treated with azithromycin and hydroxychloroquine. The patient developed multiple episodes of large volume diarrhea requiring a fecal management system. Five days later, she developed rectal bleeding with bright blood. Her hemoglobin dropped from 10.5 to 6.7 g/dL. Rectal examination revealed bright red blood mixed with melena. The patient remained hemodynamically stable and received 2 units of packed red cells. The fecal management system was removed, and she was managed conservatively with PPI as upper GIB was a differential diagnosis. Rectal bleeding resolved without needing further intervention. However, after a prolonged hospital stay, her respiratory status worsened with the change of code status to do not resuscitate. She died on hospital day 31. Demographics, clinical and laboratory parameters of 3 patients are summarized in Table 1.

DISCUSSION

Although COVID-19 is primarily a respiratory infection, GI symptoms such as nausea, vomiting, abdominal pain, and diarrhea have been reported in the range of 16%–35% patients (4). GI epithelial cells express angiotensin-converting enzyme 2 (ACE2), which is a viral entry receptor. It is unclear if SARS-CoV-2 can damage GI epithelium and cause ulceration and bleeding. Recent case series of GIB in COVID-19 suggested that conservative management led to good outcomes without a need for intervention at least in the first 24 hours (5). Although not established, the etiology of GIB is likely an anastomotic ischemic ulcer in patient 1 with RYGB, a gastroduodenal source in patients 2, and a rectal ulcer or direct trauma related to the fecal management system in 3rd patient. In our case series, 2 out of 3 patients had higher Glasgow-Blatchford bleeding score of 7 and 11 on admission which translates to high-risk GIB with a need for intervention >50%. However, both young patients responded to conservative management with careful monitoring of hemodynamic parameters, hemoglobin and hematocrit levels, and transfusion of PRBC as needed and medical therapy. Two patients died due to respiratory failure although GIB resolved.

Endoscopic evaluation is generally performed for diagnostic and therapeutic purposes in hospitalized patients with GIB; however, several factors should be carefully considered in patients with SARS-CoV-2 with GIB. First, the risk of potential exposure of endoscopy and anesthesia staff during endoscopic procedures is substantial in the setting of COVID-19 (6). This is primarily because SARS-CoV-2 spreads through droplets resulting in airborne transmission due to inherently increased risk of aerosolization during endoscpic procedures. Second, multiple GI societies have recommended to defer all elective procedures and carefully consider risk-benefit ratio for urgent procedures (7). Patient 1 was in respiratory failure requiring 15 L supplemental oxygen via a nonrebreather mask and inadvertently would require endotracheal intubation and ventilatory support during the endoscopic procedure and perhaps longer duration after. If the need for endoscopic procedure with high aerosolization risk is inevitable, caution is warranted for the medical staff involved in the procedure with proper appropriate personal protective equipment including face shield, double gloves, use of N95 masks, and careful "donning and doffing" technique to limit the risk of exposure (8). Third, because of the current pandemic, conservation of personnel and resources is crucial. For these patients, a conservative approach is suggested in the setting of GIB, and if endoscopic intervention is unlikely to improve the outcome (too sick or stable). Large cohort or case-control studies and risk scoring models in the future may provide further insight into optimal management of GIB in patients with SARS-CoV-2.

CONFLICTS OF INTEREST

Specific author contributions: C.G. and A.P. were responsible data acquisition, review of literature, and drafting and approval of the final manuscript. All authors were involved in the final approval of the version of the manuscript submitted and have agreed to be accountable for all aspects of the work.
Financial support: None to report.
Potential competing interests: None to report.

REFERENCES

1. The Lancet. Emerging understandings of 2019-nCoV. The Lancet 2020;395:311.
2. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China. Am J Gastroenterol 2020;1 (http://journals.lww.com/10.14309/ajg.0000000000000620).
3. Luo S, Zhang X, Xu H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). Clin Gastroenterol Hepatol 2020;18(7):1636–7.
4. Nobel YR, Phipps M, Zucker J, et al. Gastrointestinal symptoms and COVID-19: Case-control study from the United States. Gastroenterology (http://www.ncbi.nlm.nih.gov/pubmed/32294477). (2020). Accessed April 19, 2020.
5. Cavaliere K, Levine C, Wander P, et al. Management of upper GI bleeding in patients with COVID-19 pneumonia. Gastrointest Endosc (https://linkinghub.elsevier.com/retrieve/pii/S001651072034181X) (2020). Accessed April 19, 2020.
6. Han J, Wang Y, Zhu L, et al. Preventing the spread of COVID-19 in digestive endoscopy during the resuming period: Meticulous execution of screening procedures. Gastrointest Endosc 2020;3:3855.
7. Castro Filho EC, Castro R, Fernandes FF, et al. Gastrointestinal endoscopy during COVID-19 pandemic: An updated review of guidelines and statements from international and national societies. Gastrointest Endosc 2020;3:3854.
8. Repici A, Maselli R, Colombo M, et al. Coronavirus (COVID-19) outbreak: What the department of endoscopy should know. Gastrointest Endosc 2020;3:019.