Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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LETTER TO THE EDITOR

Self-limited gastrointestinal bleeding in COVID-19

KEYWORDS
COVID-19;
SARS-2-CoV;
Melena;
Hematochezia;
Gastrointestinal bleeding

Introduction

Over 3.5 million people worldwide have been infected with SARS-CoV-2 [1]. SARS-CoV-2, a single-stranded RNA virus of the beta coronavirus genus enters the body via the angiotensin converting enzyme 2 (ACE2) receptor [2,3]. ACE2 is expressed in gastrointestinal (GI) epithelial cells suggesting that SARS-CoV-2 can infect and replicate in the GI tract [4]. Studies have identified viral RNA in stool specimens of infected patients [3]. The most prevalent GI features of COVID-19 include abdominal pain, nausea, vomiting, and diarrhea. There is limited data regarding GI bleeding in patients with COVID-19. We present a case series of six patients, most without a known source of GI bleeding, who tested positive for SARS-CoV-2 and concurrently suffered from hematochezia or melena.

Methods

This single-centered, retrospective case series was conducted at Albert Einstein Medical Center in Philadelphia and was approved by the institutional review board. We recorded cases of SARS-CoV-2 infection and concurrent GI bleeding from March 1, 2020 to April 24, 2020. SARS-CoV-2 was confirmed with a polymerase chain reaction test on sputum or nasopharyngeal swab samples.

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Results

Case #1

A 77-year-old African American female with a history of lung cancer, diabetes, hypertension, and dementia presented with hematochezia and hypotension. She had a history of internal hemorrhoids and diverticulosis. Labs showed a hemoglobin of 8.0 g/dL (baseline 9.0 g/dL), elevated inflammatory markers, and positive SARS-CoV-2 test. On hospital day 4, the patient was intubated for hypoxia. Pulmonary angiogram showed a sub-segmental pulmonary embolism and a heparin drip was initiated. She required two units of blood. Her bleeding stopped without intervention. She expired due to hypoxic respiratory failure.

Case #2

A 77-year-old African American male with a history of diabetes, hypertension, and prostate cancer presented with shortness of breath, abdominal pain, and hematochezia. Labs showed elevated inflammatory markers, including D-Dimer, and positive SARS-CoV-2 status. The patient received supplemental oxygen and therapeutic enoxaparin due to his elevated D-Dimer. His hemoglobin remained stable and oxygen requirements decreased prior to discharge home.

Case #3

A 66-year-old Hispanic female with a history of chronic obstructive pulmonary disease and peripheral arterial disease presented for endarterectomy. On hospital day 15, she developed shortness of breath, fever, tachycardia, and melena. SARS-CoV-2 test was positive. Her hemoglobin remained stable and she had no further melena prior to discharge.

Case #4

A 66-year-old African American male with a history of end stage renal disease, hypertension, diabetes, coronary artery disease, recent diagnosis and treatment for confirmed

Table 1 Demographics, presentation, and laboratory values.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	77	77	66	66	76	73
Gender	Female	Male	Female	Male	Male	Male
Race	African-American	African-American	Hispanic	African-American	Caucasian	African-American
Co-morbidities	Lung cancer on chemotherapy, type 2 diabetes mellitus, hypertension, and dementia	Type 2 diabetes Mellitus, hypertension, history of prostate cancer Status post prostatectomy	COPD, peripheral arterial Disease, rheumatoid arthritis	ESRD, hypertension, hyperlipidemia, diabetes, coronary artery disease, recent diagnosis and treatment for COVID-19 complicated by pulmonary embolism, recent heparin-induced thrombocytopenia	HTN, COPD, dementia, ductal breast cancer status post treatment with Tamoxifen	HTN, dementia, GERD, seizure disorder
Home anticoagulation	None	None	None	Eliquis	None	Started on Xarelto at nursing home upon positive COVID-19 test
GI history	Internal hemorrhoids, large and small diverticular disease, and small hiatal hernia	None	None	None	None	None
Symptoms on presentation	Hematochezia and hypotensive episode	Shortness of breath, abdominal pain and hematochezia for one weeks duration	Left limb ischemia and left greater toe ulcer	One episode of melena	Shortness of breath and melena	Shortness of breath
White blood cells (10^3/mcL)	6.66	9.34	9.21	9.78	20.20	5.59
Platelets (10^3/mcL)	247	319	506	310	492	216
Hemoglobin on admission (g/dL)	8.0	14.9	8.4	12.9	9.5	9.8
Hemoglobin at baseline (g/dL)	9.0	15.0	9.5	13.0	13.5	12.5
PT (sec)	15.4	15.9	12.6	21.3	18.3	14.4
INR	1.2	1.2	0.9	1.8	1.5	1.1
CRP (mg/L)	104.9	45	N/A	91.4 (3 days prior to admission)	44.9	N/A
Ferritin (ng/mL)	959	595	110	11,589 (3 days prior to admission)	282	51
D-Dimer (ng/mL)	4,150	13,500	N/A	3,370	3,760	730
COVID-19 Status	Positive	Positive	Positive	Positive	Positive	Positive
Highest required FiO2	Intubated, 100% FiO2	15L via non-rebreather mask	room air	2L via nasal cannula	2L via nasal cannula	Intubated, 100% FiO2
Endoscopic intervention	None	None	None	None	None	EGD without intervention

SARS-CoV-2 infection complicated by pulmonary embolism and heparin-induced thrombocytopenia (HIT) on apixaban presented with melena. Labs revealed hemoglobin of 13.0 g/dL and elevated inflammatory markers. The patient's hemoglobin remained stable and he was discharged.

Case #5

A 76-year-old Caucasian male with a history of dementia and breast cancer presented with shortness of breath and melena. SARS-CoV-2 testing was positive. His melena stopped on hospital day 4 and his hemoglobin stabilized without endoscopic intervention.

Case #6

A 73-year-old African American male with a history of hypertension, dementia, gastroesophageal reflux disease and seizures who was found at his nursing home to be COVID positive and started on rivaroxaban, presented with hypoxia. Labs showed an elevated troponin and he was transitioned to a heparin drip. He had melena on hospital day 2 and heparin was discontinued. He was intubated for hypoxia on hospital day 3. Bedside endoscopy showed no gross abnormality. His hemoglobin stabilized and he was started on enoxaparin for DVT prophylaxis. He was extubated and continues inpatient treatment with remdesivir.

Discussion

GI manifestations such as decreased appetite, abdominal pain, nausea, vomiting and non-bloody diarrhea have been reported in 3-50% of patients with SARS-CoV-2 [3]. There is limited published literature describing GI bleeding as a symptom of SARS-CoV-2 infection. ACE2 receptors are found throughout the GI tract, allowing the virus to gain entry into GI host cells, replicate, and cause an inflammatory response[4,5]. One case report describes an elderly female with SARS-CoV-2 infection and hematochezia, Imaging showed colitis and colonoscopy revealed patchy erythematous areas without ulceration in the left colon. Biopsy demonstrated expansion of the lamina propria by edema with normal cellularity and intact crypts without microscopic changes to indicate infectious colitis, ischemia, or inflammatory bowel disease [6].

Our case series describes six patients (Table 1), with GI bleeding and COVID-19. Four patients had bleeding occur concurrently with more common COVID-19 symptoms suggesting the virus may have played a role in causing the hemorrhage, possibly by infecting GI epithelial cells and causing mucosal damage. Based on the levels of inflammatory markers and oxygen requirements in our patients, GI bleeding does not seem to correlate with the degree of inflammation or the severity of COVID-19.

Endoscopy is a virus-aerosolizing procedure that has been used judiciously during the pandemic. Diagnostic studies implicating the virus in GI pathology have been infrequent. It is possible that the bleeding observed in the above cases is not related to COVID-19, and rather due to unknown pre-existing GI pathology. Patient #6 underwent upper endoscopy, which did not show any abnormalities. Because the onset of typical COVID-19 symptoms was accompanied by self-limited GI bleeding in five of the six cases, a correlation should be considered.

Coagulopathy is associated with SARS-CoV-2 infection. Studies have suggested a mortality benefit in anticoagulating patients with elevated D-dimer [7]. Because of the increased risk of thrombi and disseminated intravascular coagulation, hospitalized patients have been placed on therapeutic anticoagulation [8]. Among our patients, patients #4 and #6 were on anticoagulation prior to experiencing bleeding. Patient #4 had no history of bleeding and was taking apixaban for two weeks due to HIT. Patient #6 had bleeding after starting prophylactic rivaroxaban. Given the possible increased risk of bleeding in COVID-19, therapeutic anticoagulation in infected patients should be used cautiously.

This case series shows a possible increased risk of bleeding among patients with COVID-19. Further study of how SARS-CoV-2 affects the GI tract is warranted. Areas of research may include assessing for mucosal damage, evaluating a correlation with inflammatory markers and reviewing additional cases of bleeding in COVID-19 patients.

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Disclosure of interest

The authors declare that they have no competing interest.

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Lisa F. Barrett[a,*]
Kevin Bryan Lo[a]
Steven R. Stanek[b]
James W. Walter[b]

[a] *Department of Internal Medicine, Einstein Healthcare Network, 19141 Philadelphia, USA*
[b] *Department of Gastroenterology, Einstein Healthcare Network, 19141 Philadelphia, USA*

* Corresponding author.
E-mail addresses: barrettl@einstein.edu (L.F. Barrett), lokevinb@einstein.edu (K.B. Lo), stanekst@einstein.edu (S.R. Stanek), walterja@einstein.edu (J.W. Walter)
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