

[ CASE REPORT ]

## A Rare Case of COVID-19 Pneumonia Concomitant with Bleeding from Acute Gastric Mucosal Lesions

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### Abstract:

A 70-year-old man was diagnosed with coronavirus disease 2019 (COVID-19) pneumonia. Twenty-six days after admission, he experienced hematemesis despite improvement in his respiratory symptoms. Contrast-enhanced computed tomography revealed edematous stomach wall thickening with neither ischemic findings in the gastric wall nor obstruction of the gastric artery. Emergent esophagogastroduodenoscopy showed diffuse dark-red mucosa accompanied by multiple easy-bleeding, irregularly shaped ulcers throughout almost the whole stomach without active bleeding or visible vessels. The clinical course, including the endoscopic findings, progressed favorably with conservative treatment. COVID-19 pneumonia can present with acute gastric mucosal lesion, which may be induced by microvascular thrombosis due to COVID-19-related coagulopathy.

**Key words:** coronavirus disease 2019, COVID-19, gastrointestinal bleeding, acute gastric mucosal lesion

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### Introduction

The coronavirus disease 2019 (COVID-19) outbreak has spread worldwide, with more than 121 million cases and more than 2 million deaths reported (1). Japan has also been affected by this virus, with over 454,000 cases reported in Japan, including 8,790 deaths (2).

Respiratory symptoms, including a fever and cough, are typical in COVID-19-positive patients. However, the prevalence of gastrointestinal (GI) symptoms was reported to be 15% (range: 2-57%), with nausea and vomiting, diarrhea, and loss of appetite being the most common such symptoms (3). Upper GI hemorrhaging can also occur, being reported in 2% of patients with GI manifestations (4), caused mainly by GI ulcers, erosive/hemorrhagic gastritis, erosive/ulcerative diffuse damage, and esophagitis (5-10). These symptoms can be induced by drugs, including steroids, non-steroidal anti-inflammatory drugs and anti-platelets, stress,

*Helicobacter pylori* infection, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

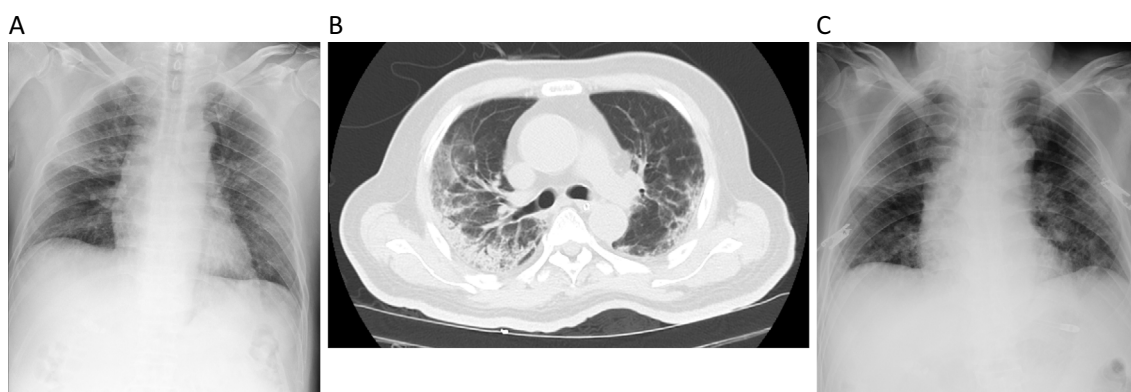
SARS-CoV-2 enters the body via the angiotensin-converting enzyme 2 (ACE2) receptor, which is also expressed in extrapulmonary organs, including the GI tract (11, 12). In a meta-analysis, the pooled prevalence of stool samples positive for virus ribonucleic acid (RNA) was 48.1%; among these samples, 70.3% of those collected after the disappearance of the virus from respiratory specimens tested positive for the virus (13). These findings show that GI symptoms can be induced by a direct viral inflammatory response, potentially via the fecal-oral transmission route (13, 14).

We herein report a rare case of COVID-19 pneumonia concomitant with bleeding from an acute gastric mucosal lesion (AGML) wherein the clinical course was able to be endoscopically observed.

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**Figure 1.** A: A posterior-anterior chest radiograph showed ground glass and linear opacities in the mid and lower zones in the periphery of both lungs. B: Chest computed tomography showed bilateral subpleural consolidations. C: Ground glass and linear opacities in the mid and lower zones of both lungs remained on a posterior-anterior chest radiograph obtained before esophagogastroduodenoscopy.

**Table.** Laboratory Findings of the Present Case before and after Hematemesis.

	Day 25	Day 27		Day 25	Day 27
Hematology			Blood chemistry		
WBC	9,790	13,200 / $\mu$ L	TP	5.4	5.8 g/dL
RBC	339	400 $\times 10^4$ / $\mu$ L	T-Bil	1.0	1.1 mg/dL
Hemoglobin	10.3	12.2 g/dL	AST	44	26 IU/L
Hematocrit	30.2	37.1 %	ALT	70	58 IU/L
Platelets	19.0	22.5 $\times 10^4$ / $\mu$ L	LDH	278	395 IU/L
			$\gamma$ -GTP	67	66 IU/L
Coagulation			Amylase	625	801 IU/L
PT	50.8	63.1 %	BUN	20.1	28.5 mg/dL
APTT	75.4	47.7 s	Creatinine	0.57	0.71 mg/dL
D-dimer	3.4	7.2	CRP	1.81	2.41 mg/dL

WBC: white blood cell count, RBC: red blood cell count, PT: prothrombin time, APTT: activated partial thromboplastin time, T-Bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine transaminase, LDH: lactate dehydrogenase,  $\gamma$ -GTP:  $\gamma$ -glutamyltransferase, BUN: blood urea nitrogen, CRP: C-reactive protein

## Case Report

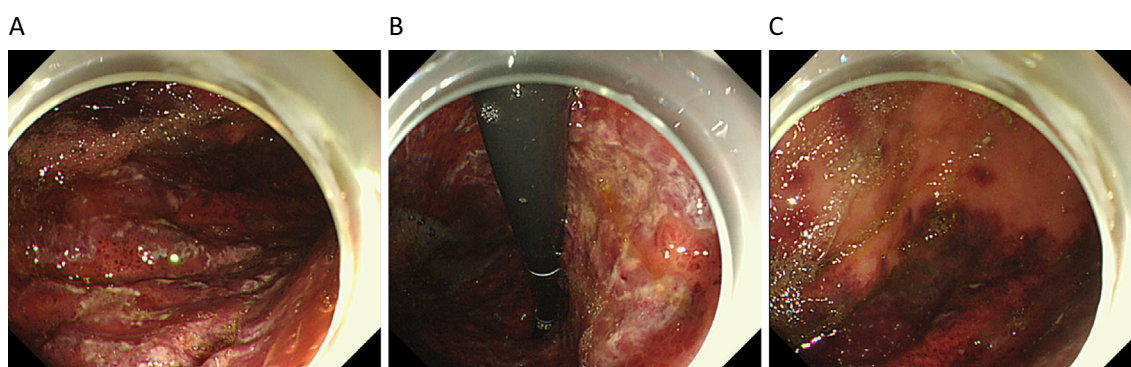
The patient was a 70-year-old man with a medical history of diabetes mellitus and hyperlipidemia who was suffering from COVID-19 pneumonia (Fig. 1A, B). He had regularly taken vildagliptin (100 mg per day), voglibose (0.4 mg per day) and rosuvastatin calcium (2.5 mg per day), which were continued after admission. His respiratory distress improved 20 days after being treated with intravenous dexamethasone sodium phosphate, nafamostat mesilate, ceftriaxone sodium hydrate, sulfamethoxazole trimethoprim (ST) mixture, and remdesivir under management with a transient artificial respirator. He then started tubal feeding with the administration of intravenous dexamethasone sodium phosphate (6.6 mg per day), perioral vonoprazan fumarate (10 mg per day), perioral ST mixture, and continuous intravenous heparin sodium (17,000 unit/day) for thromboprophylaxis.

The patient presented with hematemesis six days after

starting these treatments. His laboratory data (Table) revealed strong inflammatory changes (white blood cells: 13,200/ $\mu$ L, C-reactive protein level: 2.41 mg/dL), a hypercoagulability state (D-dimer: 7.2  $\mu$ g/mL), and no progression of anemia (hemoglobin level: 12.2 g/dL). Reverse-transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2 of oropharyngeal swabs had been negative two days before hematemesis. Ground glass and linear opacities in the mid and lower zones of both lungs remained on a posterior-anterior chest radiograph (Fig. 1C). Contrast-enhanced computed tomography (CT) revealed edematous stomach wall thickening; however, neither ischemic findings in the gastric wall nor obstruction of the gastric artery was detected (Fig. 2). Emergent esophagogastroduodenoscopy (EGD) showed diffuse dark-red mucosa accompanied by multiple easy-bleeding irregular-shaped ulcers in almost the whole stomach without either active bleeding or visible vessels (Fig. 3A, B). This lesion looked segmental, and borderline findings between dark-red and a normal appearance



**Figure 2.** Contrast-enhanced computed tomography revealed edematous stomach wall thickening. Neither ischemic findings in the gastric wall nor obstruction of the gastric artery was detected.



**Figure 3.** A, B: Emergent esophagogastroduodenoscopy showed diffuse dark-red mucosa accompanied by multiple easy-bleeding irregularly shaped ulcers throughout almost the whole stomach without either active bleeding or visible vessels. C: The lesion looked segmental, and borderline findings between dark-red and a normal appearance were clearly recognized at the antrum.

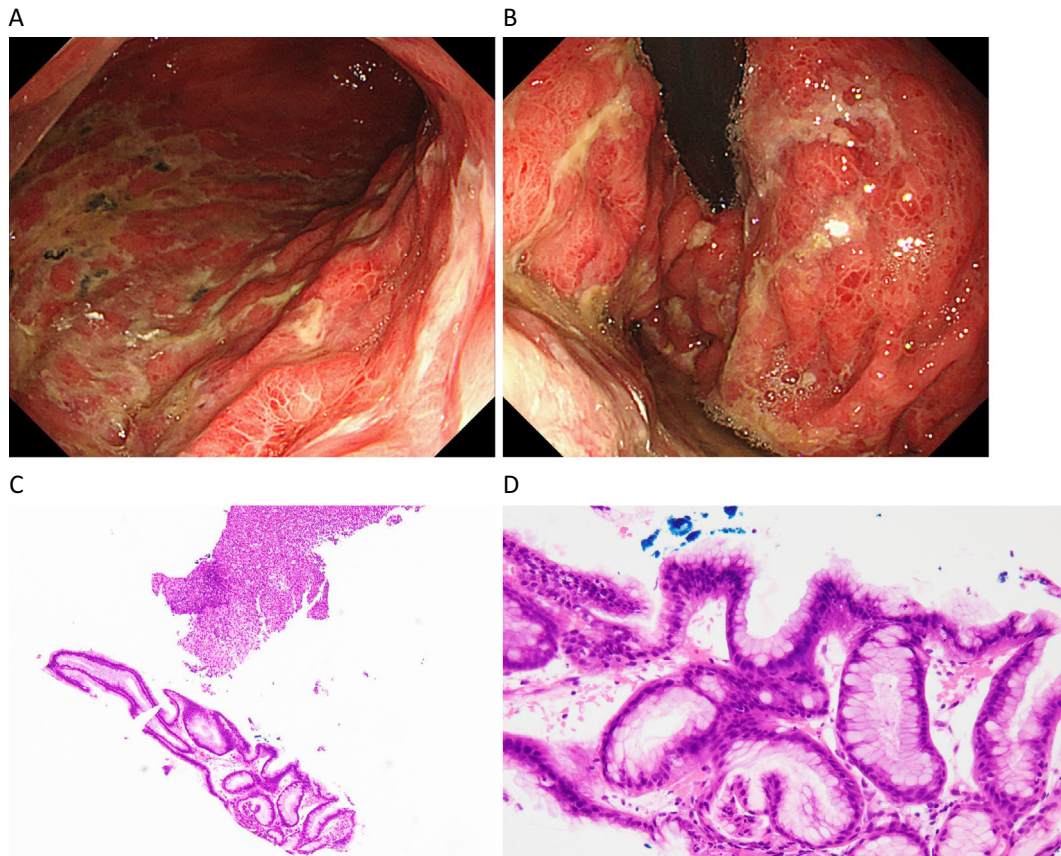
were clearly recognized at the antrum (Fig. 3C). No abnormalities in other parts of the digestive tract or other organs suggestive of microvascular thrombosis were revealed on contrast-enhanced CT or EGD. EGD was performed by an endoscopist who was assisted by two endoscopic personnel wearing personal protective equipment (face shield, surgical mask, isolation gown, and disposable gloves) in our negative-pressure endoscopy room. The endoscope was used, washed and disinfected while taking particular care to avoid contamination. All of the health care personnel working in the endoscopic unit were confirmed to be negative for COVID-19 infection by RT-PCR tests performed the next day and one month after the EGD procedure.

After starting treatment, including fasting, parenteral nutrition, the administration of intravenous omeprazole sodium 40 mg per day, and the discontinuation of intravenous heparin sodium, hemostasis was achieved. Ten days after starting the treatment, the gastric mucosal lesion was endoscopically improved (Fig. 4A, B), with a histopathological examination revealing non-specific, benign ulcers without *H. pylori* in-

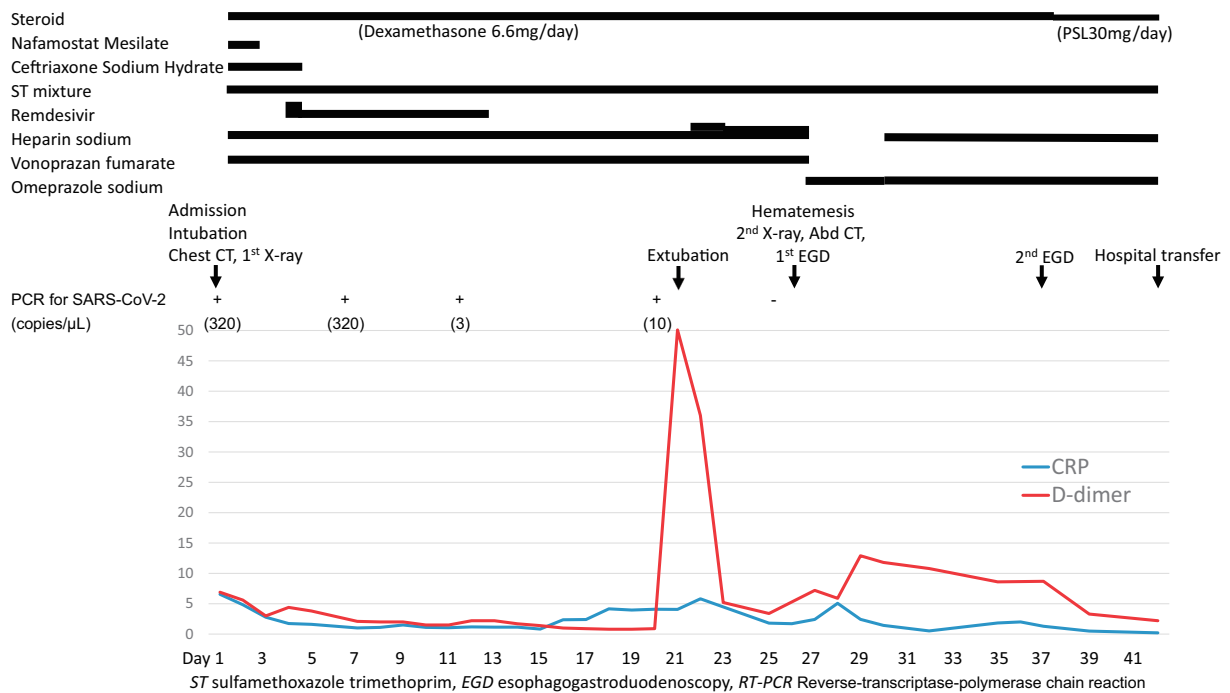
fection (Fig. 4C, D). He has experienced neither abdominal symptoms nor rebleeding events since then. His clinical course is summarized in Fig. 5.

## Discussion

Erosive and ulcerative diffuse damage can cause GI bleeding in patients with COVID-19, with a reported incidence of 16% in the upper and 33% in the lower GI tract (5). However, a diffuse appearance, such as ischemic changes in the upper GI, has never been reported. Vanella et al. (5) presented a case with a bleeding gastric ulcer with irregular margins in the lesser curvature accompanied by small duodenal ulcers. The histology of the gastric ulcer showed ischemic damage with sporadic endocapillary microthrombi. The coagulation changes associated with COVID-19 suggest the presence of a hypercoagulable state that might increase the risk of thromboembolic complications (15). Indeed, a histological examination of postmortem tissue revealed evidence of microvascular thrombosis in the



**Figure 4.** A, B: The gastric mucosal lesion was endoscopically improved 10 days after starting the treatment. C, D: A biopsy specimen taken from the gastric mucosal lesion showing exudates with neutrophil infiltration and a superficial gastric mucosa accompanied by regenerative change and mild lymphocytic infiltration in the stroma, indicating non-specific, benign ulcers (Hematoxylin and Eosin staining, C:  $\times 40$ , D:  $\times 200$ ).



**Figure 5.** Clinical course of the patient.

skin and lungs (16). Furthermore, an increased D-dimer concentration is one of the most typical findings in patients with COVID-19 and coagulopathy, as shown in our present case (15). An endoscopic appearance of segmental dark-red mucosa and ulcers can also suggest diffuse mucosal ischemia. Risk factors that can induce AGML, including shock, sepsis, respiratory failure, renal failure, and hepatic failure were able to be denied at the onset of hematemesis, and gastric acid hypersecretion due to stress was not likely to have occurred as the patient had been regularly taking a potassium-competitive strong acid blocker in Vopran (17). Therefore, such ischemic mucosal damage in the GI tract can be induced by microvascular thrombosis associated with coagulopathy due to COVID-19 infection.

Other causes that can present similar image findings, such as acute phlegmonous gastritis and drug-induced gastritis, also needed to be differentiated in this case. However, these conditions were able to be excluded based on the endoscopic findings of no pus excretion and segmental mucosal damage as well as lack of medical changes over the previous three weeks.

*H. pylori* negativity was histopathologically confirmed. However, the possibility of *H. pylori* infection cannot be completely ruled out as a pin-point diagnosis of bacterial infection using a single sample obtained under the administration of antibiotics may have induced a false-negative result.

According to the guidelines for the management of non-variceal upper GI bleeding (18-20), early upper GI endoscopy within 24 hours of presentation following hemodynamic resuscitation is recommended. However, the indication of urgent GI endoscopy should be limited in patients with COVID-19 pneumonia. Endoscopic procedures themselves may cause the deterioration of the respiratory condition, resulting in the need for intubation with general anesthesia. Furthermore, endoscopy is an aerosol-producing procedure and thus associated with a risk of viral transmission to healthcare workers in the endoscopy unit. According to guidelines published by Western and Japanese GI-associated societies (21-24), a patient presenting with upper GI bleed should undergo EGD within 24 hours of the symptom onset. However, European guideline conversely state that GI endoscopy procedures for upper GI bleeding without hemodynamic instability warrant a case-by-case evaluation based upon medical necessity (22). Cavaliere et al. (25) proposed that endoscopy be reserved if a patient does not respond to conservative treatment, including a proton pump inhibitor drip, blood transfusion as needed, and frequent monitoring of vital signs, GI symptoms, and hemoglobin values within 24 hours. However, according to the guideline of the Japan Gastroenterological Endoscopy Society, the patient is considered to have been cured and normal endoscopy can be performed if 10 days have passed since the onset and 72 hours have passed since the symptoms were relieved, even in symptomatic patients with confirmed SARS-CoV-2 infection (23). In our present case, it was considered that COVID-19 pneumonia had already been cured when the pa-

tient began vomiting blood, as 26 days had passed from the onset of COVID-19 pneumonia and 6 days had passed since his respiratory symptoms had been relieved. Furthermore, we confirmed a negative result for SARS-CoV-2 by RT-PCR before endoscopy. However, we should pay close attention when performing endoscopy even in such situations, as virus RNA in stool samples often remains positive even after the disappearance of the virus from respiratory specimens (13).

The clinical course, including the endoscopic findings progressed favorably with conservative treatment, suggesting that the microvascular ischemic damage of the gastric mucosa had been transient, as in ischemic colitis. The accumulation of more cases will be required in order to discuss the indication of urgent endoscopy if diffuse GI wall thickening indicating COVID-19-related coagulopathy, is revealed on ultrasonography or CT.

In conclusion, COVID-19 pneumonia can present with AGML, which may be induced by microvascular thrombosis due to COVID-19-related coagulopathy. The accumulation of more case is needed in order to develop a management strategy for GI bleeding in patients with COVID-19 pneumonia.

**The authors state that they have no Conflict of Interest (COI).**

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