Upper Gastrointestinal Bleeding Caused by SARS-CoV-2 Infection

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INTRODUCTION
Since the novel coronavirus (SARS-CoV-2) (1) spread across the world, evidence has emerged that the gastrointestinal tract may be a potential transmission route and target organ (2). Of 98 patients with SARS-CoV-2 infection at our institution, 1 patient developed upper gastrointestinal bleeding during hospitalization, the diagnosis and management of which are described below.

CASE REPORT
A 77-year-old man from Wuhan, China, with no previous gastrointestinal illness was admitted to our hospital with a 6-day history of fever, cough, and fatigue. He was diagnosed with SARS-CoV-2 infection after evaluation and testing (3). His infection progressed rapidly, and tracheal intubation and mechanical ventilation were required on hospital day 4.

On hospital day 10, he acutely developed coffee-ground emesis with a decrease in the hemoglobin level indicative of upper gastrointestinal bleeding. With continued bleeding despite intravenous octreotide (25 µg/h) and esomeprazole (8 mg/h) infusions and nasogastric administration of a traditional Chinese mucosal protective agent (Yunnan white drugs 0.5, 4/d), urgent gastroscopy was deemed necessary and was performed 12 hours later.

On inspection of the esophagus, multiple round herpetic erosions and superficial ulcers (4–6 mm in size) were visualized in the proximal esophagus (Figure 1). The surface of erosions and ulcers of these lesions had white exudate and blood clots. The lesions themselves were friable and bled easily on contact. Specimens were collected from esophageal lesions and peripheral blood for SARS-CoV-2 RNA detection. The tissue specimens tested positive for SARS-CoV-2 RNA, with lymphocytic infiltration typical of viral esophagitis. The remainder of the examination was normal. This confirmed that the esophageal lesions and upper gastrointestinal bleeding were caused by SARS-CoV-2 infection of the esophagus.

After gastroscopy, a nasogastric tube was positioned with the tip at the level of the esophageal lesions. A topical mucosal protective agent (aluminum phosphate gel, 20 g three times a day) and hemostatic therapy (thrombin, formulated as 16 U/mL in ice-cooled water, 50 mL every 2 hours) were administered through the nasogastric tube for 72 hours, although the head of bed was raised 30° to prevent reflux, and some of the infused medications could have flowed into the stomach. Bleeding stopped within 48 hours, but despite escalation of respiratory support, the patient died of respiratory failure on hospital day 33.

DISCUSSION
We describe for the first time an unusual case of esophageal mucosal lesions caused by SARS-CoV-2 resulting in upper gastrointestinal bleeding. The diagnosis was confirmed by virus RNA detection in the esophageal lesions. Although endoscopic hemostasis was not possible because of diffuse friability, bleeding stopped with topical mucosal protective and hemostatic agents administered via a nasogastric tube, along with systemic octreotide and esomeprazole infusions. We can draw several conclusions from this case.

First, we conclusively demonstrate that SARS-CoV-2 can infect the esophagus and can cause mucosal lesions, potentially from the virus binding to ACE2 protein expressed by gastrointestinal cells (4). We found multiple round herpetic erosions and superficial ulcers in the esophagus, with lymphocytic infiltration, which is consistent with the endoscopic and histopathologic characteristics of viral esophagitis (5). Our findings indicate that when patients with SARS-CoV-2 infection develop upper gastrointestinal bleeding, infectious esophagitis from SARS-CoV-2 needs to be considered in addition to other potential etiologies of bleeding (5). It is unknown whether other parts of the gastrointestinal tract can be similarly involved with SARS-CoV-2 infection.

Second, endoscopic hemostasis could not be achieved because of diffuse erosions, friability, and bleeding in the esophageal lesions. Instead, we continued intravenous octreotide and proton pump inhibitor therapy, and we infused a topical mucosal protective agent (aluminum phosphate gel) and iced thrombin solution through a nasogastric tube positioned at the level of the esophageal lesions. Thrombin can promote platelet aggregation and can generate stable fibrin through the coagulation cascade to promote coagulation, which we have found useful when endoscopic hemostasis is not possible. Therefore, although supportive management can be of value, endoscopic therapy may not be possible.

Finally, because we isolated SARS-CoV-2 viral RNA from the esophageal lesions, it will be of utmost importance for endoscopy personnel to pay close attention to adequate personal protective equipment and measures to mitigate exposure when performing endoscopic procedures in patients infected with SARS-CoV-2. In addition, endoscopes and operating instruments should be thoroughly cleaned and disinfected to avoid cross infection.

In summary, upper gastrointestinal bleeding caused by SARS-CoV-2 is a new and important challenge for gastroenterologists with implications on potential for spread of infection through endoscopy.

CONFLICTS OF INTEREST
Guarantor of the article: Hong Shan, MD, PhD, supervised the study and accepts full responsibility for the integrity of the work as a whole.

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responsibility for the conduct of the study, and he has had access to the data and have control of the decision to publish.

**Specific author contributions:** X.L. designed the study and revised the draft. S.H., R.L., Z.Z., and X.L. planned and conducted the study. X.Z. collected and interpreted data. J.L. drafted the manuscript.

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