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Don't Overlook Digestive Symptoms in Patients With 2019 Novel Coronavirus Disease (COVID-19)

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In late December 2019, a cluster of patients with pneumonia of unknown cause was linked epidemiologically to a seafood and wet animal wholesale market in Wuhan City, China. The causative pathogen subsequently was identified as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Over the course of the current pandemic, it became apparent that some patients can present with abdominal symptoms without fever or respiratory manifestations, and could be overlooked by health care providers.

We present a case series of hospitalized patients with SARS-CoV-2 infection whose initial symptoms were gastrointestinal.

Methods

This retrospective study was approved by the Medical Ethical Committee of Zhongnan Hospital of Wuhan University. We evaluated all 1141 cases of 2019 novel coronavirus disease (COVID-19) admitted to Zhongnan Hospital of Wuhan University from January 1, 2020, to February 20, 2020. A diagnosis of COVID-19 pneumonia was based on the COVID-19 Prevention and Control Program (4th edition) published by the National Health Commission of China.²

All patients received chest computed tomography (CT) and had throat-swab specimens obtained and maintained in viral-transport media. Reverse-transcription polymerase chain reaction detection reagents were provided by the Center for Disease Control and Prevention, Wuhan, Hubei Province. Laboratory confirmation of COVID-19 was performed both in our hospital and the Center for Disease Control and Prevention laboratory of Hubei Province. Confirmed cases of COVID-19 infection were defined as those with a positive test result from either laboratory.³

Results

Of 1141 confirmed COVID-19 cases, 183 (16%) presented with gastrointestinal symptoms only, and their clinical characteristics are summarized in Table 1. Men slightly outnumbered women, and the most common gastrointestinal symptom was loss of appetite, followed by nausea and vomiting, which occurred in

approximately two thirds of cases. Diarrhea and abdominal pain were the presenting symptom in 37% and 25% of patients, respectively.

Laboratory testing showed that mean leukocyte ($2.7 \pm 0.2 \times 10^9/L$) and lymphocyte ($0.53 \pm 0.014 \times 10^9/L$) counts were below normal, and C-reactive protein levels were increased (18.7 ± 6.8 mg/L). Mild increases in serum aminotransferases were noted (aspartate aminotransferase, 65.8 ± 12.7 U/L; alanine aminotransferase, 66.4 ± 13.2 U/L), but renal function generally was intact.

At the onset of their illness, 175 of 183 (96%) of patients had lung lesions on chest CT, which were unilateral in 61% of cases. The most common CT findings were abnormal lung texture (83%), ground-glass densities (73%), consolidation (27%), and pleural effusion (11%).

The mean time elapsed for confirmation of COVID-19 was 3.5 days from the onset of symptoms. Of the 183 patients, 7 died of progressive respiratory failure, and 176 recovered.

Discussion

Patients with COVID-19 typically present with fever or a respiratory syndrome. Our case series shows that some patients can present with gastrointestinal symptoms, with a paucity of other manifestations. Such patients could be overlooked, leading to potentially serious consequences to them and their contacts. It is important that clinicians are aware that COVID-19 can present with predominantly gastrointestinal symptoms, and maintain appropriate vigilance and a high index of suspicion.

SARS-CoV-2 can enter angiotensin converting enzyme II (ACE2)-expressing cells. ACE2 is expressed not only in lung AT2 cells, but also can be found in the upper esophagus, and in stratified epithelial cells and absorptive enterocytes in the ileum and colon.⁴ The enteric symptoms of SARS-CoV-2 may be associated with invaded ACE2-expressing enterocytes.⁵ These findings

Abbreviations used in this paper: ACE2, angiotensin converting enzyme II; COVID-19, 2019 novel coronavirus disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Table 1. Patients With COVID-19 Infection Presenting With Gastrointestinal Symptoms

Clinical characteristics/cases (N = 183)	N (%)	P value
Sex		.032
Male	102 (56)	
Female	81 (44)	
Age, y, means ± SD	53.8	
Epidemiologic history		.063
Environmental exposure	94 (51)	
Close contact	99 (54)	
Gastrointestinal symptoms		
Nausea	134 (73)	
Vomiting	119 (65)	
Abdominal pain	45 (25)	
Diarrhea	68 (37)	
Loss of appetite	180 (98)	
Both nausea and vomiting	37 (20)	
Both abdominal pain and diarrhea	16 (9)	
All symptoms	12 (7)	
Laboratory characteristics		
Leukocytes, $3.5\text{--}9.5 \times 10^9/\text{L}$	2.7 ± 0.2	
Lymphocytes, $1.1\text{--}3.2 \times 10^9/\text{L}$	0.53 ± 0.014	
C-reactive protein, 0–10.0 mg/L	18.7 ± 6.8	
Aspartate aminotransferase, 15–40 U/L	65.8 ± 12.7	
Alanine aminotransferase, 9–50 U/L	66.4 ± 13.2	
Blood urea nitrogen, 2.8–7.6 mmol/L	6.4 ± 2.5	
Creatinine, 64–104 $\mu\text{mol/L}$	85.7 ± 37.2	
Chest CT findings	175	
Unilateral	107 (61)	
Bilateral	68 (39)	
Abnormal lung texture	145 (83)	
Ground-glass shadow	128 (73)	
Pulmonary consolidation	47 (27)	
Unilateral pleural effusion	13 (7)	
Bilateral pleural effusion	7 (4)	

COVID-19, 2019 novel coronavirus disease; CT, computed tomography.

suggest that the digestive system, along with the respiratory tract, may be a potential route for SARS-CoV-2 infection, and could explain why some patients present with gastrointestinal symptoms.

Much still needs to be learned about this zoonotic coronavirus that has crossed species to infect human populations,⁶ and its spectrum of disease.

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Conflicts of interest

The authors disclose no conflicts.