LETTER TO THE EDITOR

SARS-CoV-2 Infection: Beyond the Interstitial Pneumonia

Dear Editor:

Recently, we have enthusiastically read the article by Pan et al1 that was published in *Am J Gastroenterol*. The authors investigated the prevalence and outcomes of COVID-19 patients with digestive symptoms, which provided useful information for us to identify the underlying patients infected with SARS-CoV-2. Here we report 3 cases in Wuhan Leishenshan Hospital with late complications (pulmonary-cerebral thrombosis, lung abscesses, and pancreatitis) possibly due to SARS-CoV-2 infection to help recognize and treat COVID-19 better.

Case 1: A 49-year-old man was admitted to the isolation ward with a 1-month history of fever, dry cough and shortness of breath. Eight days prior, he began to have chest pain, blood-tinged sputum and left-side hemiplegia. His viral RNA tested positive. The angiography confirmed right main pulmonary artery embolism in lower right lobe. After admission, the laboratory investigations showed leukocytosis, lymphopenia and a high D-dimer concentration (Figure 1A-C). The first chest computed tomography (CT) revealed a mass shadow of high density in the lower right lobe (Figure 1D). The CT of his brain showed right frontal lobe infarction with hemorrhagic transformation (Figure 1E, yellow arrow). Five days later, the second chest CT revealed a cavitation in condensation shadows in the lower right lobe (Figure 1F). After receiving antiviral and supportive treatment, his symptoms were gradually eased.

Case 2: A 49-year-old man was admitted to the isolation ward with a nearly 2-month history of fever, cough and chest tightness. Ten days prior to admission, he began to have dyspnea. He was a light smoker and had quitted smoking for many years. Because pneumothorax occurred in his right lung, a closed chest drainage was done. Eight days later he was transferred to our hospital. On the day of admission, immediate chest CT showed a lung abscess in right middle lobe (Figure 2A, yellow asterisk). Four days later, the repeated chest CT revealed that the lung abscess was fading gradually after antiviral and antibiotic treatment (Figure 2B). His fever disappeared and dyspnea was resolved gradually.

Case 3: A 37-year-old man was referred to the general outpatient clinic with the complaints of abdominal pain in left upper quadrant for 5 days. The patient had no history of obesity, overeating, or staying up late. Two months earlier, the patient began to have dry cough without fever, chest distress, muscle ache or fatigue. His chest CT showed suspected viral pneumonia, then he was admitted to the isolation ward. The laboratory investigations showed elevated concentrations of amylase and lipase in his serum (Figure 3A). His viral RNA testing was negative in nasal or throat swabs, but the serum antibodies to SARS-CoV-2 were positive. The abdomen CT showed pancreatic edema with obscure fat spaces around the pancreas (Figure 3B, red arrows). After receiving antiviral and supportive treatment, his symptoms were relieved.

SARS-CoV-2 binds with high affinity to human angiotensin-converting enzyme 2 (ACE2) which is used as an entry receptor to invade target cells.2 It is well established that most patients with COVID-19, caused by infection with SARS-CoV-2, have fever along with respiratory signs and symptoms, such as cough and dyspnea.3 Herein, we reported 3 cases with late complications that presented at least 1-2 months after initial symptoms onset. The study suggested that COVID-19 might develop lung abscess, pancreatitis and thrombotic complications in the late stage. The underlying mechanism might be that the virus invades cells via binding to ACE2 and thereby causes organ damage.4 It is known that ACE2 is enriched in the heart, kidneys, and intestines and is also broadly distributed in the lungs, liver, intestine, and brain.5 Theoretically, any human cells expressing ACE2 may be susceptible to SARS-CoV-2 infection.

In case 1, it is speculated that the virus triumphed over the clearance of the immune system and invaded vascular endothelial cells through the ACE2 receptor, resulting in excessive inflammation, hypercoagulable state and thrombosis. High D-dimer concentration was common in patients with COVID-19 and might contribute to the thrombosis.6 In case 2, exhausted lymphocytes (figure not shown) could reduce immunity, thereby rendering the host susceptible to bacterial infection and abscess development because lymphocytes play a decisive role in maintaining immune homeostasis and inflammatory response throughout the body.7 In case 3, elevated levels of serum amylase and/or lipase were found in many patients with COVID-19 in Wuhan Leishenshan Hospital. We speculated two potential mechanisms leading to this abnormality.8 The virus might directly infect the pancreatic ductal epithelial cells, resulting in cell dysfunction.9 Pro-inflammatory cytokines (e.g., tumor necrosis factor α, interleukin -6) and inflammatory stress could lead to metabolic disorders in pancreas. Mechanisms...
FIGURE 1. Laboratory parameters in case 1 and 3 and computed tomography (CT) images of three cases.

Case 1: timeline charts illustrated leukocytosis, lymphopenia and a high D-dimer concentration (1A-C). The first CTs of chest and brain were obtained on day 12 after the onset of illness. Chest CT showed bilateral multiple mottling and ground-glass opacity. Condensation shadows were observed in the lower right lobe (1D). The CT of the brain showed right frontal lobe infarction with hemorrhagic transformation (1E, yellow arrow). The second chest CT revealed a cavity in condensation shadows in the lower right lobe (1F).

Case 2: the first and second chest CTs were obtained on day 1 and 4 after the admission, respectively. A cavitation with fluid level inside was observed in right middle lobe (2A, yellow asterisk). The red arrow indicated closed drainage tube. The second chest CT showed that the lung abscess was fading gradually (2B).

Case 3: timeline charts illustrated the elevated serum concentrations of amylase and lipase. On the day 5 after the onset of abdominal pain, the serum concentrations of amylase and lipase reached the peak (3A). The abdomen CT showed edema pancreatitis (3B, red arrows).
mentioned above or beyond might work together to cause pancreatitis.

Although the complications we report here are at a relatively low risk of occurrence, clinicians should recognize these secondary diseases earlier to implement timely assessment and treatment when fighting against this pandemic.

Ran Cui, MD\textsuperscript{1,2,**}

Yu-Lan Wang, MD\textsuperscript{3,**}

Jing Li, MD\textsuperscript{4}

Sheng-Ming Dai, MD, PhD\textsuperscript{1,*}

\textsuperscript{1}Department of Rheumatology and Immunology, Shanghai Jiao Tong University Affiliated Sixth People’s Hospital, Shanghai, China

\textsuperscript{2}Department of Infectious Diseases, Wuhan Leishenshan Hospital, Wuhan, Hubei Province, China

\textsuperscript{3}Molecular Diagnostic Laboratory of Cancer Center, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

\textsuperscript{4}Department of Radiology, Shanghai Jiao Tong University Affiliated Sixth People’s Hospital, Shanghai, China

\textsuperscript{*E-mail: shengmingdai@163.com

\textsuperscript{**}Ran Cui and Yu-Lan Wang contributed equally.

Conflicts of Interest: All authors declare that they have no conflicts of interests.

Ethics Statement: This is a case series report, all patients in this study have been anonymized.

REFERENCES


