DOI: 10.1002/jmv.26134

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

Pancreatic injury in the course of coronavirus disease 2019: A not-so-rare occurrence

To the Editor,

We read with interest the review by Liu and Liu regarding the management of coronavirus disease 2019 (COVID-19). Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) emerged by the end of 2019 and rapidly spread throughout the world.

As of 24 May 2020, more than 5 000 000 confirmed infections have been reported worldwide, with over 300 000 deaths.

Although respiratory symptoms are typically found during the course of COVID-19, as reported in the article of Liu and Liu,[1] gastrointestinal manifestations are also being increasingly observed.[2]

Moreover, data regarding COVID-19-associated pancreatic injury are still limited. Recently, Wang et al[3] found that 17% of 52 patients with COVID-19 pneumonia showed pancreatic injury without clinical signs of severe pancreatitis. Meanwhile, Hadi et al[4] reported severe acute pancreatitis in two first-line relatives in course of COVID-19.

So far, the mechanisms underlying COVID-19 induced-pancreatic damage have not been completely understood. It has been hypothesized that SARS-CoV-2 may use angiotensin-converting enzyme 2 receptors, highly expressed in pancreatic islet cells, to gain cellular entry, thus resulting in a direct cytopathic effect.[5]

TABLE 1 Clinical features of the six patients with pancreatic abnormalities

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6
Sex	F	M	M	M	M	M
Age, y	90	49	41	56	68	67
Comorbidities	Hypertension, dementia, and osteoporosis	N	N	N	Hypertension	Hypertension
Pancreatic function test at admission	Abnormal	Normal	Normal	Normal	Normal	Normal
Time from onset symptoms to hospitalization, days	8	7	10	12	7	7
Time from admission to pancreatic injury, days	NA	6	6	2	7	9
Serum total amylase peak, U/L	562	223	194	202	730	119
Serum lipase peak, mean, U/L	2430	1025	812	831	3445	511
Altered transaminase during hospitalization	Y	Y	Y	Y	Y	Y
Pneumonia	Y	Y	Y	Y	Y	Y
Oxygen support	Y	Y	Y	N	Y	Y
Treatment						
HDQ+ LPV/r	N	Y	Y	Y	Y	Y
Antibiotics	Y	Y	N	N	Y	Y
Tocilizumab	N	N	N	N	Y	N
Steroids	N	Y	N	N	Y	N
Complications	ARDS and MOF	ALI	ALI	N	ARDS	ALI
Transferred to ICU	N	N	N	N	Y	N
Outcome						
Discharged	N	Y	Y	Y	Y	Y
Death	Y	N	N	N	N	N
Days of hospitalization	5	22	11	12	39	24

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; F, female; HDQ, hydroxychloroquine; ICU, intensive care unit; LPV/r, lopinavir/ritonavir; M, male; MOF, multiple organ failure; N, No; NA, not available; Pt, patient; Y, Yes.

On the contrary, the pancreatic injury might depend on several indirect events including cytokine storm, immune response, as well as endothelial dysfunction, leading to a process called "viral sepsis," addressed to the multiple organ failure (MOF).[6]

Whether direct cytopathic effect may be mainly responsible for pancreatic injury, this represents a debated question deserving further investigations.

Considering this, among the 70 patients with documented COVID-19 hospitalized in our Infectious Diseases Unit from 25 February to 10 May 2020, six individuals (8.5%) showed pancreatic abnormalities (PAs) without a history of alcohol abuse, gallstones, chronic biliary, or pancreatic diseases and were included in this retrospective observational study. Clinical and biochemical data including serum amylase (normal range, 10-100 U/L) and lipase (normal range, 73-393 U/L) were collected during the hospitalization. Hyperlipasemia was defined as an elevated lipase level above the upper limit of normal (>393 U/L). Clinical features are summarized in Table 1. The median age was 56 years. Gastrointestinal symptoms were common among the six patients with PA, including four with nausea, two with anorexia, three with general abdominal discomfort, and three with diarrhea.

PAs were observed at hospital admission in only one case, whereas the remaining five showed an increase in amylase and lipase during the hospitalization, after a median period of 6 days since the admission. A slight rise of liver enzymes was also observed in all cases. Intravenous fluid therapy was promptly started along with antiviral treatment.

All six individuals had pneumonia, five of whom requiring oxygen support. In five subjects, acute respiratory failure occurred, evolving in acute respiratory distress syndrome in two cases, of whom a 90-year-old female who died developing MOF and a 68-year-old man who was transferred to the intensive care unit due to the necessity of mechanical ventilation. In both cases, elevated serum lipases were found, 2430 and 3445 U/L, respectively. Only the man underwent an abdominal CT showing no radiological signs of acute pancreatitis. However, no patient met diagnostic criteria for acute pancreatitis according to the Atlanta classification.[7] Finally, all five patients were discharged with complete regression of PA. Our observations are in agreement with the recent study of Wang et al reporting pancreatic injury without criteria for clinically severe pancreatitis.

Although elevated lipase levels have been associated with non-pancreatic etiologies, including gastritis/gastroparesis and enteritis/colitis,[8] we hypothesized that pancreatic damage may be related to several factors including the direct effect of SARS-CoV-2, inflammatory cascade, dehydration, and multiple organ dysfunction. Moreover, several drugs have been rarely associated with pancreatic damage.[9] In addition, hypertriglyceridaemia, an important risk factor for pancreatitis, has been associated with lopinavir/ritonavir in patients with HIV.[10] In our group, one patient showed slight hypertriglyceridaemia (311 mg/dL).

Therefore, it is of paramount importance to implement the knowledge of the COVID-19-associated pancreatic injury, and drug-induced toxicity should be also taken into account as an additional risk factor for developing pancreatic damage. Strict monitoring of pancreatic parameters should be performed during the management of COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

All authors contributed to writing and editing the manuscript.

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