Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Pancreatology 20 (2020) 1017–1018

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

SARS-COV-2 associated acute pancreatitis: Cause, consequence or epiphenomenon?

Keywords:
COVID-19
Pancreatitis

Dear Editor,

The rapid spread of a novel coronavirus disease (COVID-19) caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2) has triggered a global pandemic. With most patients presenting with respiratory symptoms, there is a relative paucity of knowledge about the impact of COVID-19 on the gastrointestinal tract. In the early phases of the pandemic, there appeared to be no known link between the SARS-CoV-2 virus and the pancreas. Since then, however, there have been several reports of acute pancreatitis (AP) in COVID-19 patients.

Wang et al. were the first to describe this in a case series of 52 patients, 9 of whom were diagnosed with AP [1]. Another study found elevated amylase and lipase levels in 12 of 64 patients with severe COVID-19 infection [2]. The severity of AP observed varies from mild [1,2] to severe [3] but unfortunately accepted diagnostic criteria [4] was not used in these studies, raising the possibility that the elevated pancreatic enzymes may be due to other causes including increased gut permeability with SARS-CoV-2 infection [5]. Not only is there the possibility of over-reporting SARS-CoV-2 associated AP, there could also be under-reporting. The recently formed Consortium for Clinical Characterisation of COVID-19 comprising 96 hospitals across five countries has generated a database of anonymised electronic health records from 21,324 patients [6]. Of the 34 patients with a diagnosis of AP, 24 did not have a stated cause. Further, 20% of patients with COVID-19 infection present with abdominal symptoms and a proportion of these may represent a missed diagnosis of AP, especially when attention is diverted to the management of critically ill patients with multiple organ failure.

Not only is there uncertainty about the incidence of SARS-CoV-2 associated AP but there are also questions about its clinical features and pathogenesis. We do not know the timing of AP in relation to SARS-CoV-2 inoculation or the natural history and clinical trajectory of SARS-CoV-2 associated AP. It is not known whether currently accepted prognostic scoring systems for AP are appropriate, whether there is a heightened pro-inflammatory response, or whether the risk of organ dysfunction (especially acute respiratory distress syndrome) is compounded and/or more severe. When available, it will be interesting to study the impact of future vaccines and novel therapeutics designed for SARS-CoV-2 on the clinical course of AP.

Acute pancreatitis associated with viral infections, most commonly the hepatitis B virus and Coxsackie B virus, is well described [7]. The mechanism by which AP develops following viral infections varies depending on the type of virus involved [7]. SARS-CoV-2 is known to enter cells by binding to the receptor proteins ACE2 and TMPRSS2. A study from 2010 using immunostaining found ACE2 to be highly expressed in islet cells and postulated that binding of SARS-CoV caused islet cell injury and hyperglycaemia in infected patients [8]. Single-cell RNA sequencing has been used to evaluate their expression, but there is conflicting data with one study reporting high expression within ductal and acinar cells [3], while another study found no significant expression in the pancreas [9]. It is not known whether SARS-CoV-2 causes AP, whether the AP is a consequence of severe systemic inflammation and microvascular thrombosis from COVID-19 infection, or whether it is just an epiphenomenon.

More data about SARS-CoV-2 associated AP is needed from both the laboratory and the clinic. One way forward might be to use a pancreas organoid model to study the pancreas-specific effects of SARS-CoV-2, analogous to the intestinal organoid model used to study enteric infections [10]. There is also an urgent need for more international collaboration to pool clinical and scientific experience about SARS-CoV-2 associated AP, to better understand it and to improve the management of these patients.

Acknowledgements

The authors have no conflicts of interest or financial support to declare.

References

[1] Wang F, Wang H, Fan J, et al. Pancreatic injury patterns in patients with COVID-19 pneumonia. Gastroenterol. Pub. Online First. 1 Apr 2020. https://doi.org/10.1053/j.gastro.2020.03.055.
[2] Liu F, Long X, Zhang B, et al. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clin. Gastroenterol. Hepatol. Pub. Online Frist 22 Apr 2020. https://doi.org/10.1016/j.cgh.2020.04.040.
[3] Hadi A, Werge M, Kristiansen KT, et al. Coronavirus Disease-19 (COVID-19) associated with severe acute pancreatitis: case report on three family members. Pancreatol. Pub. Online Frist 5 May 2020. https://doi.org/10.1016/j.pan.2020.04.021.
[4] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[5] Zhang H, Kang Z, Gong H, et al. Digestive system is a potential route of COVID-19: an analysis of single-cell coexpression pattern of key proteins in viral entry process. Gut 2020;69:1010–8.

https://doi.org/10.1016/j.pan.2020.05.019

[6] Brat GA, Weber GM, Gehlenborg N, et al. International electronic health record-derived COVID-19 clinical course profiles: the 4CE Consortium. medRxiv 30 Apr 2020. https://doi.org/10.1101/2020.04.13.20059691. Published Online First.
[7] Rawla P, Bandaru SS, Vellipuram AR. Review of infectious etiology of acute pancreatitis. Gastroenterol Res 2017;10(3):153–8.
[8] Yang J, Lin S, Ji X, et al. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol 2010;47:193–9. 2010.
[9] Sungnak W, Huang N, Bécavin C, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat Med 2020;26:681–7.
[10] Zhou J, Li C, Liu X, et al. Infection of bat and human intestinal organoids by SARS-CoV-2. *Nat Med* Published Online First 13 May 2020. https://doi.org/10.1038/s41591-020-0912-6.

Glenn Kunnath Bonney*, Yujia Gao, Claire Alexandra Chew
Department of Surgery, National University Hospital, Singapore

John Albert Windsor
Department of Surgery, National University Hospital, Singapore

HBP/Upper GI Unit, Auckland City Hospital/Department of Surgery, University of Auckland, New Zealand

* Corresponding author. National University Hospital, 1E Kent Ridge Rd, 119228, Singapore.
E-mail address: glenn_bonney@nuhs.edu.sg (G.K. Bonney).

19 May 2020
Available online 29 May 2020