DOI: 10.1111/liv.14540

SARS-CoV-2 as an extrahepatic precipitator of acute-on-chronic liver failure

To the Editor

We read with great interest the report by Qiu et al[1] reporting the first case of acute-on-chronic liver failure (ACLF) following SARS-CoV-2 infection. Based on elevated transaminases, jaundice and coagulopathy, the authors discuss hepatic virus entry and systemic inflammation as possible underlying mechanisms.[1] As ACLF following hepatic vs extrahepatic insults may differ in presentation, course and prognosis,[2] we herein report the case of a patient with ACLF precipitated by extrahepatic complications of SARS-CoV-2.

A known 65-year-old male with non-alcoholic steatohepatitis (NASH) cirrhosis and ascites was admitted to hospital following nausea, vomiting, reduced food intake and diarrhoea for the past 2 days. The patient did not report respiratory symptoms. Initial laboratory workup showed leucocytosis (16.0 × 10^9/L) with lymphopenia (4%), renal failure (creatinine 937 µmol/L) defining ACLF grade 1, and worsening jaundice (bilirubin 198 µmol/L). Notably, serum levels of alanine aminotransferase and lactate dehydrogenase were not increased, while aspartate aminotransferase was mildly elevated (103 U/L). Spontaneous bacterial peritonitis was excluded and microbiological cultures from blood and urine remained sterile. Broad-spectrum antibiotics were initiated. CT scan showed multiple consolidations suspicious for COVID-19 pneumonia (level 4 according to the COVID-19 Imaging Reporting and Data System; Figure 1A). Nucleic acid testing for SARS-CoV-2 from nasopharyngeal swabs was marginal positive (cycle threshold value 36) but negative in repeating samples. Criteria for respiratory failure were not fulfilled at any time.

Diagnostic work-up revealed hepatorenal syndrome-type acute kidney injury (HRS-AKI). After initial renal replacement therapy for hyperkalaemia, terlipressin and albumin were administered. Urine analysis was not suggestive for COVID-19-associated intrinsic AKI.[3] Recurrence of HRS-AKI required a second treatment with terlipressin/albumin resulting in complete response 19 days after admission (Figure 1B). Immunoglobulin G antibodies against SARS-CoV-2 became positive 25 days after admission in EUROIMMUN ELISA. After temporary improvement in renal function, ACLF progressed to grade 2 following catheter-associated urinary tract infection and haemorrhagic complications after abdominal paracentesis, and the patient underwent liver transplantation 28 days after admission.

Although definite data are still lacking, patients with cirrhosis are considered at a greater risk for severe COVID-19. This case illustrates how SARS-CoV-2, which can productively infect enterocytes[4] and renal glomerular epithelial, endothelial and tubular cells,[5] may precipitate ACLF that is predominantly driven by renal failure. In addition to hepatic injury, hepatologists should carefully note intestinal symptoms and monitor renal function in patients with cirrhosis at risk of COVID-19, even in the absence of respiratory symptoms.

Karsten Große[1]
Matthijs Kramer[2]
Christian Trautwein[1]
Tony Bruns[1]

[1]*Department of Internal Medicine III, University Hospital RWTH Aachen, Aachen, Germany*
[2]*Maastricht University Medical Centre (MUMC), Maastricht, The Netherlands*

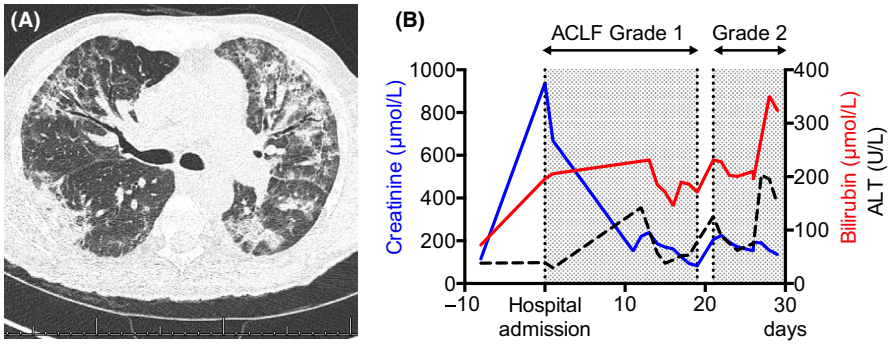

FIGURE 1 A, Chest CT on admission showing multiple central and peripheral pulmonary consolidations suspicious for COVID-19 (level 4 according to the COVID-19 Imaging Reporting and Data System). B, The courses of alanine aminotransferase (ALT, black dashed), total serum bilirubin (red line), and serum creatinine (blue) and the severity of acute-on-chronic liver failure (ACLF) according to EF CLIF criteria are shown

Correspondence

Tony Bruns, Department of Internal Medicine III, University Hospital RWTH Aachen, Pauwelsstraße 30, 52074 Aachen, Germany.

Email: tbruns@ukaachen.de

ORCID

Tony Bruns https://orcid.org/0000-0002-5576-6914

REFERENCES

1. Qiu H, Wander P, Bernstein D, Satapathy SK. Acute on chronic liver failure from novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Liver Int*. 2020, in press. https://doi.org/10.1111/liv.14506
2. Shi YU, Yang Y, Hu Y, et al. Acute-on-chronic liver failure precipitated by hepatic injury is distinct from that precipitated by extrahepatic insults. *Hepatology*. 2015;62:232-242. https://doi.org/10.1002/hep.27795
3. Pei G, Zhang Z, Peng J, et al. Renal involvement and early prognosis in patients with COVID-19 pneumonia. *JASN*. 2020. https://doi.org/10.1681/ASN.2020030276
4. Lamers MM, Beumer J, van der Vaart J, et al. SARS-CoV-2 productively infects human gut enterocytes. *Science*. 2020. https://doi.org/10.1126/science.abc1669
5. Puelles VG, Lütgehetmann M, Lindenmeyer MT, et al. Multiorgan and renal tropism of SARS-CoV-2. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMc2011400