



Post-COVID-19 cholangiopathy

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In our clinical experience with the Gamma variant in Brazil, we have come across many cases of this novel clinical entity. There was one case in 2020 that has left a mark in our practice, published in the beginning of 2021 in Portuguese (1). A 63-year-old male previously healthy patient developed a severe case of coronavirus disease 2019 (COVID-19) respiratory disease, needing prolonged mechanical ventilation and high-dose vasopressor drugs. He was admitted to the hospital on April 27, 2020. He was treated with multiple antibiotics during his stay, the last ones were an association of imipenem, polymyxin B and amikacin for a New Delhi metallo-beta-lactamase (NDM) *Pseudomonas aeruginosa* infective endocarditis. He underwent an endoscopic retrograde cholangiopancreatography (ERCP), which found a choledochal cast, composed of microlithiasis in the pathology report. He also underwent a percutaneous transhepatic cholangiography, which showed sclerosing cholangitis associated with intrahepatic lithiasis. He was discharged on September 25, 2020 with liver transplantation referral. After a couple of weeks of the hospital discharge, he was readmitted with a new severe sepsis, and the family opted for palliative care, and died not long afterwards. We believe this might be the first case

reported of this entity, with extensive workup, including ERCP and percutaneous transhepatic cholangiography (PTHCh), showing the presence of casts and lithiasis in the intra and extra-hepatic biliary tract, which makes this case unique. As based in the article by Roth *et al.* (2), we have put together a table summarizing our data (*Table 1*).

COVID-19 infection might cause liver injury, which is generally mild and transient. Although, in more severe cases, the patients might develop an entity entitled “post-COVID-19 cholangiopathy”. In 2021, two articles published in the American Journal of Gastroenterology discussed in total 15 cases of this disease (2,3). The case described had a cast removed in ERCP and we found one case similar to ours published in 2022 (4). It has been suggested that the diagnosis and management of this disease might demand an ERCP, especially if a dilated choledocus is identified in imaging studies (5,6). An actual cause is yet to be determined, but it is believed that it might be secondary to infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus or by drug-induced liver injury, since these patients sometimes use ketamine and carbapenems for long periods of time (7). Since we know so little of this entity, diagnosis and

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Table 1 Summary of the reported case

Clinical characteristics of patients with severe cholangiopathy during recovery from COVID-19	Reported case data
Patient demographics	
Age (years)	63
Sex	Male
Ethnicity/race	Caucasian
Hypertension	No
Diabetes mellitus	No
Other pre-existing comorbidities	No
Clinical characteristics of COVID-19 infection	
Hospitalizations	Day 1–151
Acute rehabilitation	No
Subacute rehabilitation	No
Mechanical ventilation and tracheostomy	Yes
Venovenous extracorporeal membrane oxygenation	No
Vasopressor support	Yes
Biventricular systolic heart failure	No
Acute kidney injury	Yes → hemodialysis
Renal replacement therapy	Yes
Secondary infections	<i>Pseudomonas aeruginosa</i> endocarditis
Other notable complications	Infection by <i>Candida albicans</i>
Hydroxychloroquine	No
Azithromycin	Yes
Ivermectin	No
Corticosteroids	Yes
Tocilizumab	No
Anakinra	No
Convalescent plasma	Yes
Remdesivir	No
Antibiotics	Azithromycin, Ampicillin + Sulbactam, Imipenem, Levofloxacin, Meropenem, Piperacillin, Polymyxin B, Trimethoprim, Sulfamethoxazole and Vancomycin
Liver chemistries (serum) on admission (day 1)	
Antifungal medications	Fluconazole
Alkaline phosphatase (U/L)	202
Aspartate aminotransferase (U/L)	111
Alanine aminotransferase (U/L)	39
Total bilirubin (mg/dL)	25.20
Peak liver chemistries (serum)	
Alkaline phosphatase (U/L)	936 (day 46)
Aspartate aminotransferase (U/L)	378 (day 46)
Alanine aminotransferase (U/L)	690 (day 46)
Total bilirubin (mg/dL)	31.9 (day 96)

Table 1 (continued)

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Characteristics	Reported case data
Last available liver chemistries (serum)	
Days after initial admission	Day 173
Alkaline phosphatase (U/L)	238
Aspartate aminotransferase (U/L)	105
Alanine aminotransferase (U/L)	78
Total bilirubin (mg/dL)	30.9
Hepatobiliary imaging findings	
Cirrhotic morphology	No
Hepatomegaly	No
Extrahepatic bile duct dilatation	Yes
Intrahepatic bile ducts	Dilatation, stenosis and intrahepatic lithiasis in a transhepatic percutaneous cholangiography
Endoscopic retrograde cholangiography (days after initial admission)	Choledochal casts, suggestive of microlithiasis in the pathology report
Histologic parameters	
Liver biopsy (days after initial admission)	Suggestive of drug-induced cholangitis
Portal tract findings	
Bile duct paucity (% of portal tracts with interlobular bile ducts)	Not identified
Ductular reaction	Mild
Cholangiocyte swelling (bile ducts, ductules)	Severe
Cholangiocyte regenerative change (bile ducts)	No
Portal tract inflammation (lymphoplasmacytic, with scattered neutrophils)	Mild
Hepatic arteries	Without changes
Portal veins	Without changes
Terminal hepatic veins	Without changes
Parenchyma	Without changes
Immunohistochemistry	Not done
Fibrosis	No

COVID-19, coronavirus disease 2019.

treatment for this condition are continuously revised as per available information. Symptoms, clinical signs, laboratorial manifestations, and imaging findings of the post-COVID-19 cholangiopathy do not differ from other etiological types. An adequate treatment is yet to be determined, but it seems that liver transplantation might have good results (8-11).

In conclusion, as the COVID-19 pandemic is now transforming into an endemic, we will have to manage the long-term consequences of this infection. Liver transplantation programs will require more data in this pathology, since it seems as of right now the only adequate

readily available therapy in the long term (12).

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