Untying the knot: Acute variceal bleeding in a COVID-19 patient. What should the gastroenterologist keep in mind?

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Coronavirus disease 2019 (COVID-19) has rapidly spread throughout the world, affecting medical practice. Although it usually presents with respiratory symptoms, gastrointestinal and/or liver involvement might sometimes constitute basic manifestations [1–3]. A 40-year-old male with alcoholic Child–Pugh C cirrhosis presented fever, dyspnea and worsening of liver-function tests (LFTs). He tested positive for COVID-19 and was hospitalized. His temperature was 38.5°C, he was disoriented and icteric with ascites. Laboratory values included bilirubin: 13.38 mg/dL, aspartate transaminase: 73 IU/L, gamma-glutamyl transpeptidase: 144 U/L, albumin: 1.8 g/dL. A computed tomography scan revealed mild lung involvement, ascites and varices in the hepatogastric space. The following day, the patient had episodes of hematemesis. Coagulation deteriorated (international normalized ratio from 1.02 to 3.56, fibrinogen from 443 to 152 mg/dL, activated-partial-thromboplastin time 82.1 s and D-dimers: 15 759 μg/L). He was intubated and transferred to our COVID-19- dedicated ICU, with negative-pressure chambers, for emergency endoscopy. An endoscopic tower was specially prepared for COVID-19 cases (Fig. 1). Upper gastrointestinal-endoscopy revealed esophageal varices actively bleeding; band ligation was performed, resulting in effective hemostasis. However, despite supportive care (including hydroxychloroquine and piperacillin-tazobactam), he remained febrile, LFTs and renal function deteriorated and he succumbed the next day.

Our case is a rare combination of variceal bleeding in a COVID-19 patient. Recently, 95 COVID-19 patients were reviewed for gastrointestinal manifestations [4]. Fifty-eight (49.5%), had mostly nonspecific symptoms, including anorexia/nausea in 17.9% and diarrhea (3.2% at admission and 24.2% during hospitalization).

Gastrointestinal-bleeding was rare, encountered in two patients (2.1%); these and four other patients underwent upper gastrointestinal-endoscopy; esophageal erosions and ulcers positive for the virus were found in one bleeding patient with severe COVID-19. No endoscopic interventions were undertaken. Hepatic manifestations also occur in COVID-19 [2,3]. Our patient had decompensated cirrhosis and, although evidence is scarce, COVID-19 could have affected his rapid hepatic deterioration. Hyperalbuminemia has been linked to COVID-19 severity. Could our patient’s hyperalbuminemia have been an “alarm” for his bad outcome? The association could have been via acute-on-chronic disease through direct viral hepatotoxicity, COVID-19-related disseminated intravascular coagulation or drug-hepatotoxicity [2,3]. Naturally, coexisting infection from other pathogens or random coexistence could also be the case.

Gastrointestinal-endoscopy in COVID-19 patients is a risky procedure for infection, requiring close contact with the patient, especially in active bleeding, where blood might splash on personnel and surfaces [5]. In our case, an advanced personal protective equipment was used, and endoscopy was performed in a negative-pressure room with the patient intubated, using a dedicated tower, which could ideally be stored in this room, minimizing unnecessary movements of contaminated material. A tip, which could apply for practical issues of this sort, is to plan on how these procedures will be undertaken and even to rehearse them in co-operation with hospital infectious control authorities. Such measures could guaranty the best possible outcomes for these complicated cases.
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Conflicts of interest

There are no conflicts of interest.

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COVID-19 infection, liver injury and prognosis: a suggestion

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I have read with interest the paper by Lippi et al. [1]. The Authors, through the selection of six studies, affirm that the presence of liver disease at the time of coronavirus disease 2019 (Covid-19) infection does not worsen the clinical course. Chronic liver disease was not found to be associated with increased odds of the severe form of Covid-19 [odds ratio (OR) 0.96, 95% confidence interval (CI) 0.36–2.52, \( P = 0.86 \)]. Chronic liver disease was neither significantly associated with increased odds of mortality in Covid-19 patients [OR 2.33 (95% CI 0.77–7.04) \( P = 0.30 \), Cochran’s Q, \( P = 0.23 \)]. This is understandable. Pre-existing liver disease has been reported in low percentages (from 2.3% to 11%) [2–7].

What should instead be valued is the substantial percentage of liver injury highlighted in the studies published to date during the Covid-19 infection: AST (aspartate aminotransferase) increase from 22 to 58% and alanine transaminase increase from 21% to 71%.–3.5,8–11

In fact, it is known that angiotensin-converting enzyme-2 (ACE2) expression has also been detected in the liver, especially in the bile ducts. The expression here is comparable to that present in the lung (alveolar type 2 cells). It is also present in the kidney and intestine. In the presence of liver injury, the clinical path is worse with an increase in mortality.

The incidence of liver injury with clinical aggravation varies from 30 to 62% [2,7,11,12]. In the studies of Zhang et al. [7] and Huang et al. [2], all liver injury patients deceased. Huang et al. [11] have evidenced that elevated AST levels of ICU patients (62%) was higher than non-ICU patients (25%).

The explanation is to be found in the potentiation of the cytokine tsunami that liver inflammation produces. The onset of acute on chronic liver failure (ACLF) is possible. ACLF is a condition in patients with underlying chronic liver disease with or without cirrhosis [13,14]. Sometimes chronic liver disease is not known. This is especially true in cases of alcoholic or nonalcoholic steatosis/steatohepatitis where laboratory data are often normal. Or there is only an increase in gamma glutamyl transferase and ferritin. Steatosis/steatohepatitis are fertile ground for oxidative stress and lipid peroxidation.

In real practice, the ultrasound diagnosis of hepatic steatosis is not enhanced and, therefore, it is not indicated as a pre-existing pathology. Alcohol and nonalcoholic steatosis/steatohepatitis (AS/ASH, NAFLD/NASH) are frequent conditions in the general population [15].

Pooled prevalence of NAFLD globally is 25.24% with wide geographical variation across the world (USA and North America 21–24.7% and Europe 24%) [15]. Bellentani [16] affirmed that NAFLD affects 25–30% of the general population and the risk factors are almost identical to those of metabolic syndrome.

According to new criteria in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition, the prevalence of alcohol use disorders is 20–30% in men and 10–15% in women worldwide. Steatosis is evidenced in 90% of hazardous drinkers. Fifteen percent of hazardous drinkers has normal histology, while 27, 24 and 26% has fatty liver, steatohepatitis and cirrhosis, respectively [15].

The steatosic/steatohepatitic liver is a fragile liver with high levels of cytokine and ready to welcome the Covid-19 insult with a significant inflammatory response that favours multiorgan failure [17] (Fig. 1). Paizis has demonstrated that ACE expression increases in chronic liver damage and in experimental setups of diet-induced NAFLD [18].

Furthermore, subjects with alcoholic steatosis/steatohepatitis have a weak acquired or induced immune response and a greater predisposition to both bacterial and viral lung infections [17,19].

The suggestion to Lippi et al. [1] is to re-evaluate the case history in relation to what has been previously said (asymptomatic cases of steatosis/steatohepatitis known, but not considered pre-existing liver disease). This could help us better stratify the risk of our patients.

This is especially true in elderly patients with polyopathy and polytherapy. However, antioxidant systems decrease with age [20].

It is conceivable that it will not be easy to find these data in the files (alcohol consumption, steatosis of the liver) as they are too often underestimated.

However, it can be a useful suggestion for future studies.

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