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CASE REPORT

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Hypoxemia, high alveolar-arterial gradient, and bubbles in both sides of heart: A case of hepatopulmonary syndrome in the setting of COVID-19 pandemic

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Abstract

In presence of tachypnea, digital clubbing and cyanosis in a patient with the hallmarks of chronic liver disease, hepatopulmonary syndrome should be suspected and investigated.

KEYWORDS

case report, COVID-19, digital clubbing, hepatopulmonary syndrome, hypoxemia, platypnoea and orthodeoxia syndrome

1 | INTRODUCTION

A 36-year-old man with past medical history of liver cirrhosis presented to the ED during COVID-19 pandemic peak with a history of dyspnea with minimal exertion, mild cough, and fever. SARS-CoV-2 testing was negative. ABG showed a PaO_2 of 51 mm Hg with an A-a gradient of 68 mm Hg. A targeted history revealed platypnoea-orthodeoxia syndrome. Contrast echocardiography with saline was consistent with a diagnosis of hepatopulmonary syndrome.

Current SARS-Cov-2 virus pandemic (COVID-19 pandemic) challenges physicians to find diagnosis and effective treatment for ill patients with hypoxemia. However, it is not the only cause, especially in patients with liver cirrhosis.

Hepatopulmonary syndrome (HPS) has three components: liver disease, pulmonary vascular dilatation, and a defect in oxygenation.[1] This syndrome presents insidiously and requires a high degree of clinical suspicion.

We report the clinical course of a patient, who initially presented hypoxemia in the pandemic peak, but after performing a focused history revealed severe HPS.

2 | CASE PRESENTATION

A 36-year-old Hispanic man with a past medical history of Child C cirrhosis presented in the pandemic peak with shortness of breath on minimal exertion, mild cough, and fever. His history was significant for ligation of esophageal varices and prophylactic treatment with propranolol. In emergency department (ED), he was febrile to 38°C and hypoxic, requiring supplemental oxygen. He also reported upper right quadrant abdominal pain and jaundice. On physical examination, we found tachypnoea, with normal breathing sounds and normal S1 and S2 heart sounds; no murmurs were appreciated. Abdominal distention, shifting dullness, and fluid wave test

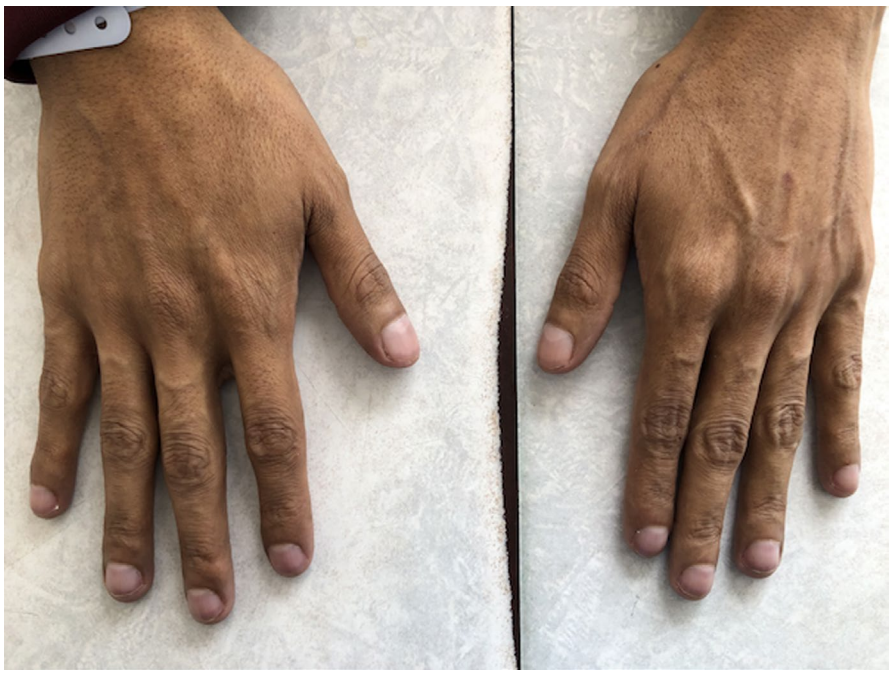

FIGURE 1 Showing clubbed fingers

were positive. Pedal edema, spider nevi, and digital clubbing were present (Figure 1). Normal mental status.

Due to COVID-19 pandemic had reached its peak and the threshold of suspicion was high, diagnostic COVID-19 tests were performed. Thoracic computed tomography (CT) scan demonstrated neither ground glass opacities nor consolidation (Figure 2 and Video S1). SARS-CoV-2 testing was negative.

Laboratories revealed lymphopenia at $0.16 \times 10^3/\mu L$ (normal $0.9\text{-}5.2 \times 10^3/\mu L$), thrombocytopenia at $24 \times 10^3/\mu L$ (normal $130\text{-}400 \times 10^3/\mu L$), C-reactive protein at 7.8 mg/dL (normal <2.0 mg/dL), and ferritin at 224 ng/mL (normal 28-365 ng/mL). ABG, performed with the patient breathing ambient air while seated, showed PaO_2 51.2 mm Hg, $PaCO_2$ 23.6 mm Hg, FiO_2 21%, PaO_2/FiO_2 243, and A-a gradient 68 mm Hg (patient temperature 37°C and 331 feet above sea level). Liver function test showed AST/ALT ratio 2.25, GGT 152 IU/L (normal 0-73 IU/L), total bilirubin 10.29 mg/dL (normal 0.3-1.2 mg/dL), conjugated bilirubin 7.16 mg/dL, prothrombin time 19.7 seconds (normal 10.5-13 seconds), and albumin 2 g/dL (normal 3.2-4.8 g/dL).

During hospitalization, he continued on oxygen via nasal cannula for oxyhemoglobin saturation of 94%. A focused history of his symptoms revealed increased shortness of breath on upright position and relieved by recumbency. Pulse oximetry in upright position was 87%, while in supine position was 92%. According to the previous findings, we suspected HPS, then a contrast-enhanced transthoracic echocardiography (TTE) with saline was performed, which showed no elevated right-sided heart pressures but abundant passage of microbubbles from the right chambers to the left chambers of the heart in the third cardiac cycle. (Figures 3-5 and Video S2).

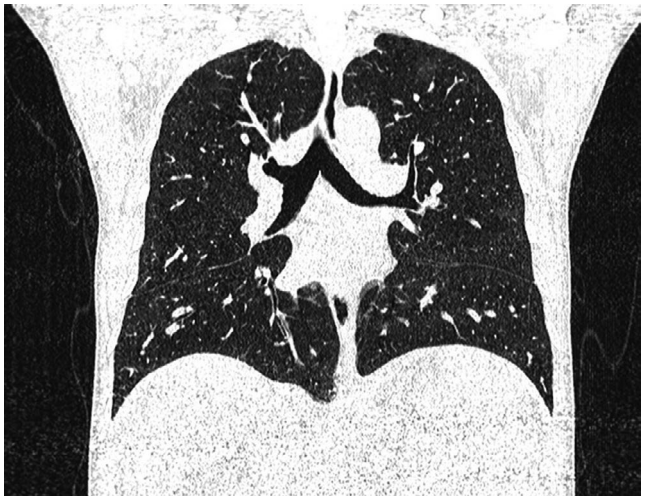

FIGURE 2 Coronal CT image. Normal chest. CT: computed tomography

Home oxygen was provided to keep saturation between 92% and 95%. Currently, the patient is in the waiting list for a liver transplant.

3 | DISCUSSION

This case is an example of an infrequent cause of hypoxemia, in contrast to the typical deoxygenation in the COVID-19 pandemic scenario, with several clues of HPS.

Hepatopulmonary syndrome is a rare condition that can cause hypoxemia with specific findings. However, it is the most common cause of respiratory insufficiency in a patient

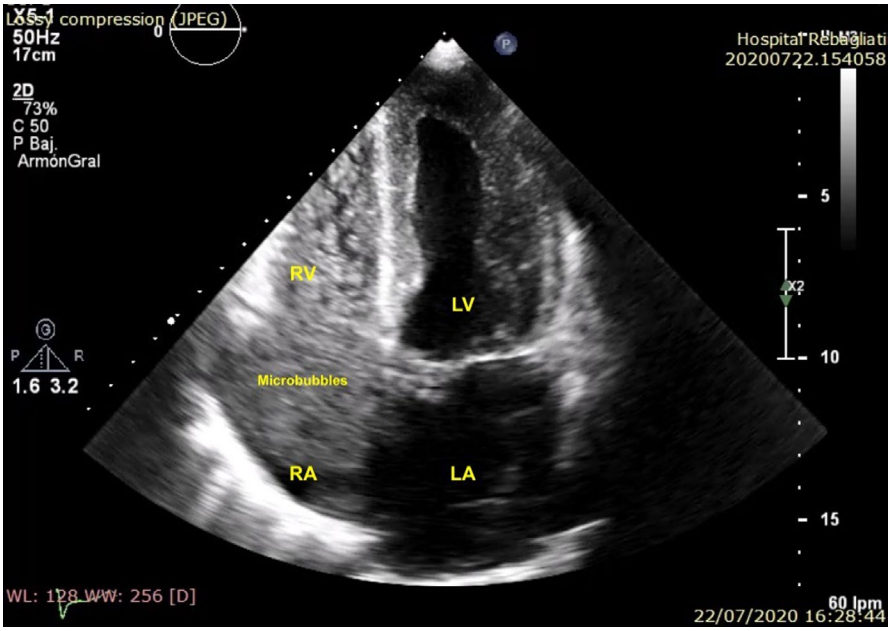

FIGURE 3 TTE, capture of apical four-chamber view at the first beat showing no bubbles in left side. TTE: transthoracic echocardiography

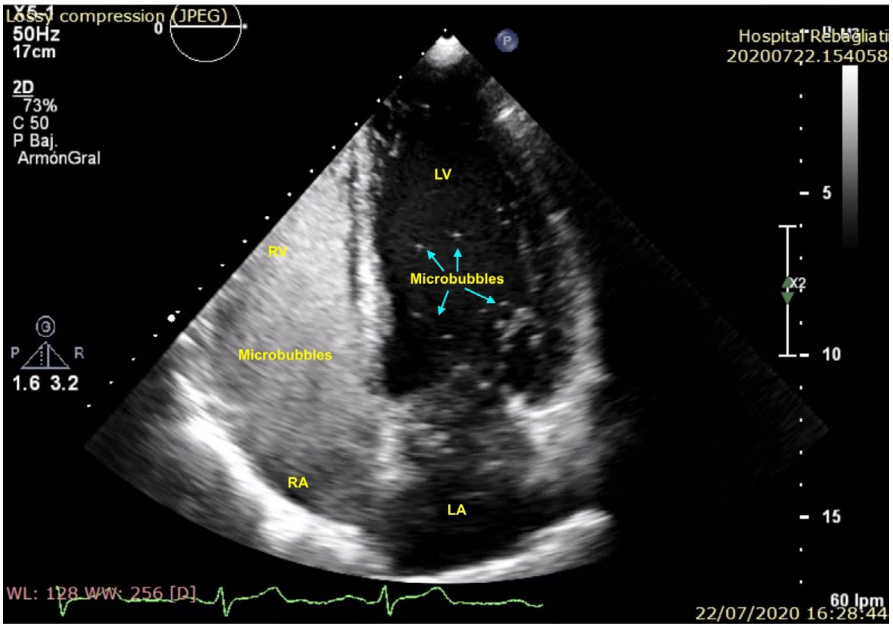

FIGURE 4 TTE, capture of apical four-chamber view at the third beat showing some bubbles in left side. TTE: transthoracic echocardiography

with a chronic liver disease (occurs in 5%-30%).[2] This syndrome is characterized by abnormal oxygenation as a result of intrapulmonary vascular dilatation.[1]

Pathogenesis in HPS is complicated.[1,3,4] The hepatic injury/failure and portal hypertension increase releasing of endothelin-1 which in turn increases expression and activity of endothelial nitric oxide synthase eliciting higher production of nitric oxide. The latter develops intrapulmonary vascular dilatations. On the other hand, bacterial translocation, portosystemic shunt, and hyperdynamic circulation produce systemic inflammation and recruitment of the macrophages in the lungs contributing to angiogenesis and vasodilation.

Alveolar-arterial gradient and the partial pressure of oxygen (>15 mm Hg and <80 mm Hg, respectively) are reasonable criteria for suspected diagnosis, while breathing room air in the sitting position at rest.[1,3] Also, the PaO2 suggests the severity of HPS. Mild HPS has a ≥80 mm Hg on air, moderate HPS has a PaO2 ≥60 and <80 mm Hg on air, severe HPS has a PaO2 ≥50 and <60 mm Hg on air, and very severe HPS has a PaO2 <50 mm Hg on air or <300 mm Hg, while the patient is breathing 100% oxygen. Our patient had a severe HPS.[1]

Platypnoea-orthodeoxia syndrome (POS) is another classic manifestation for HPS that is more specific, but not pathognomonic.[3] Platypnoea is an increase in the feeling

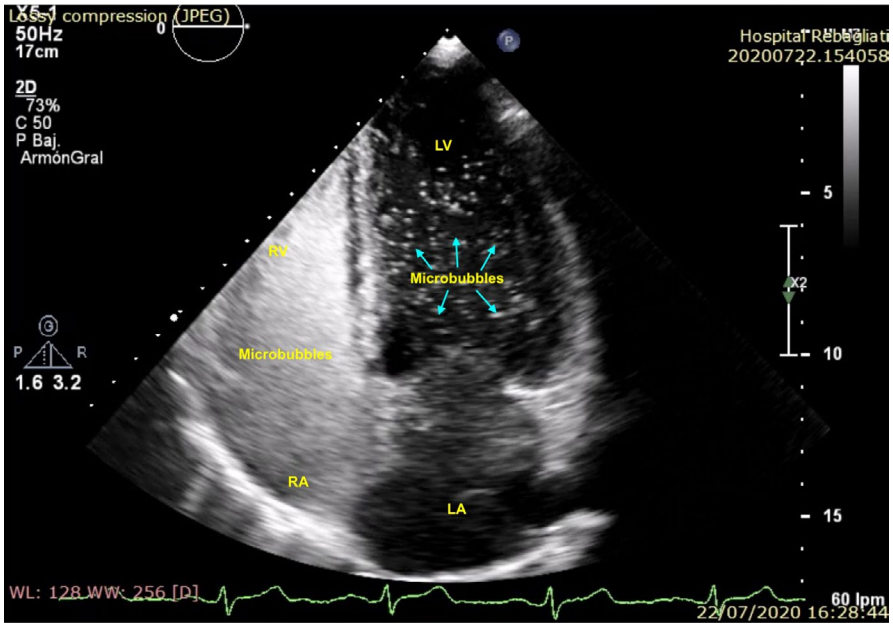

FIGURE 5 TTE, capture of apical four-chamber view at the fifth beat showing significant bubbles in left side. TTE: transthoracic echocardiography

of breathlessness when standing up, which improves when lying down. Orthodeoxia is the decrease in PaO2 (typically by more than 4 mm of Hg) or a reduction in saturations by more than 5%.[1,3] Our patient had a drop of 5%. The syndrome is also described in patients with persistent foramen ovale,[5] and the most common cause of POS is reported.[6]

Contrast-enhanced TTE to characterize HPS is recommended.[4] Furthermore, this is less invasive and more available in the midst of the COVID-19 pandemic. After the administration of agitated saline in a peripheral vein in the arm, microbubble opacification of the left atrium within three to six cardiac cycles after right-atrial opacification indicates microbubble passage through an abnormally dilated vascular bed.[7] In our patient, these findings were consistent with a diagnosis of HPS.

Long-term supplemental oxygen was highly beneficial to our patient. However, the liver transplant is the only successful treatment.[4] At the time of writing, he was in the waiting list for a liver transplant.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

JT-V: conceptualized or designed the case report. JT-V, AQ-M, and FU-M: collected the data. JT-V and AQ-M: drafted the case report. FU-M: critically revised the case report. JT-V, AQ-M, and FU-M: finally approved the version to be published.

ETHICAL APPROVAL

The author/s confirm that the written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidelines.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and/or its supplementary material. Derived data supporting the findings of this study are available from the corresponding author on request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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