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LETTER TO THE EDITOR

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Vascular liver injury mimicking an intrahepatic cholangiocarcinoma in a COVID-19 patient

To the Editor,

The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, responsible for coronavirus disease 2019 (COVID-19), has rapidly reached a pandemic spreading.

Contagion mainly occurs through the upper respiratory tract that is often involved in early disease, and pulmonary damage is the main cause of death. Nevertheless, SARS-CoV-2 can virtually localize in every organ, engendering site-specific damage.[1]

COVID-19 complications due to the prothrombotic potential associated with SARS-CoV-2 infection go beyond deep venous thrombosis and pulmonary thromboembolisms (PTEs).[2] Additional extrapulmonary tissues, such as heart, brain, and splanchnic organs, may be affected by thromboembolic events, likely originating from large vessels or due to microcirculation damage, across a wide spectrum of clinical severity.[3]

Here we report the case of a COVID-19 patient who developed PTEs, multiple floating thrombi in the aorta and splenic infarcts, as well as a large hepatic lesion, suspected for intrahepatic cholangiocarcinoma, turning out to be a sequela of portal vessel damage.

The patient, a 68-year-old man, suffered from hypertension, type II diabetes mellitus, and dyslipidemia. He was receiving atorvastatin and metformin as chronic medications. No prior thrombosis or cerebrovascular events were recorded in the past medical history.

In late March 2020, the patient was hospitalized for worsening of dyspnea and oxygen desaturation, in the context of fever and dry cough. High-resolution computer tomography (HRCT) showed lung bilateral ground-glass infiltrates, consistent with COVID-19 interstitial pneumonia (Figure 1A), and the patient tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA. High-flow oxygen therapy was started (reservoir mask at 15 L/min, fraction of inspired oxygen [FiO_2]: 80%). Main therapy consisted of hydroxychloroquine and colchicine, antibiotic and antiviral therapy, cardio aspirin 100 mg daily and enoxaparin 8000 IU daily, both as prophylaxis. Given the respiratory deterioration, a contrast-enhanced computerized tomography (CT) scan was performed. The pulmonary disease progressed to extensive consolidations in all the lobes, with a prevalent subpleural distribution, bilateral segmental pulmonary embolism was also documented. In addition, some eccentric parietal thrombi at the level of the aortic arch, descending aorta passage, descending aorta, abdominal aorta, and upper mesenteric artery were detected (Figure 1B,C). Collaterally, an irregularly, polylobulate, hypodense lesion, with ill-defined margins, was reported at the VI hepatic segment (4 × 5 cm), highly evocative for an intrahepatic cholangiocarcinoma (Figure 1D,E). Moreover, the presence of multiple infarcts (hilum and upper pole) in the spleen was recorded (Figure 1C). Given the pulmonary embolism, low-molecular-weight heparin (LMWH) posology was augmented to therapeutic dose (enoxaparin 6000 IU + 8000 IU). Liver function tests remained normal during the hospitalization. Due to the progressive clinical improvement, the patient was discharged at home on at the end of April 2020, with the indication to maintain therapy with cardio aspirin and LMWH.

In the post-hospitalization regimen 1 month after the baseline exam, the patient underwent a novel contrast-enhanced CT scan. The aortic thrombi and the splenic ischemic foci appeared significantly reduced (Figure 1B,C), while the hepatic lesion was unchanged (Figure 1D,E). As malignancy was suspected, a contrast-enhanced ultrasonography (CEUS) was performed. CEUS showed mild enhancement in the arterial phase with progressive washout and hypoechoic aspect in the portal and late vascular phase, a behavior that could not exclude a malignant diagnosis (Figure 1F,G). A liver biopsy was performed (Figure 2). The histology showed an inflammatory lesion characterized by portal-based confluent linphohistiocytic and plasma cellular infiltrates. There was no evidence of neoplasia. Alongside the clinical history of the patient, the pattern of damage was suggestive of a resolving abscess likely due to an underlying pylephlebitis, complicated by a portal venular damage sustained by an altered coagulative state.

The peculiar tropism of SARS-CoV-2 for the endothelium,[4] coupled with the perturbation of the thromboembolic homeostasis, is a major determinant in COVID-19 morbidity and mortality. In our case, we hypothesize that the splenic ischemic lesions were a consequence of the embolic sprouting of floating aortic thrombi.

The manifestations of SARS-CoV-2 can mimic a neoplastic disease, as show in the present case and by Efe et al.,[5] who surgically removed a highly symptomatic temporal mass in a young patient with the suspicion of a glial tumor, turning out to be COVID-19-related encephalitis. The clinical stability of our patient allowed a conservative approach, leading to a definitive diagnosis of a portal vasculopathy engendering extensive liver damage and excluding a cholangiocarcinoma, evoked by the radiological aspect of the hepatic lesion. Functional hepatic damage is known in COVID-19 patients,[6] while vascular damage, including portal vein thrombosis and

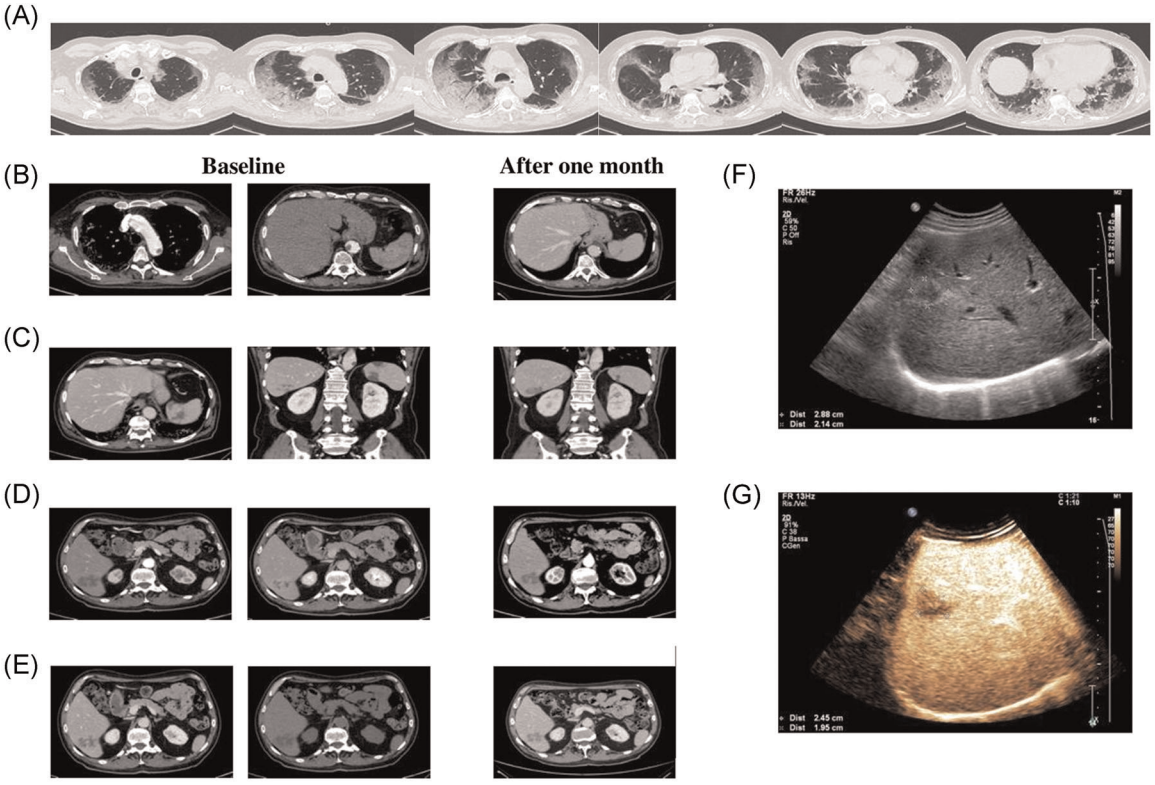

FIGURE 1 Radiologic imaging. Extensive ground-glass areas and consolidation into the "ginkgo leaf" pattern (A). Floating thrombi in the thoracic and abdominal aorta (B) were no more detectable at the follow-up CT scan, as well as splenic ischemic foci (C) were significantly reduced. No relevant radiological changes were observed between the two CT scans with regard to the hepatic lesion (D and E, representing different contrast graphic phases). B-mode ultrasound shows a focal liver lesion in VI hepatic segment as a hypoechoic focal lesion with hyperechoic margins (F). Contrast-enhanced ultrasound during the late vascular phase shows clear washout with a hypoechoic aspect of the focal lesion (G). CT, computerized tomography

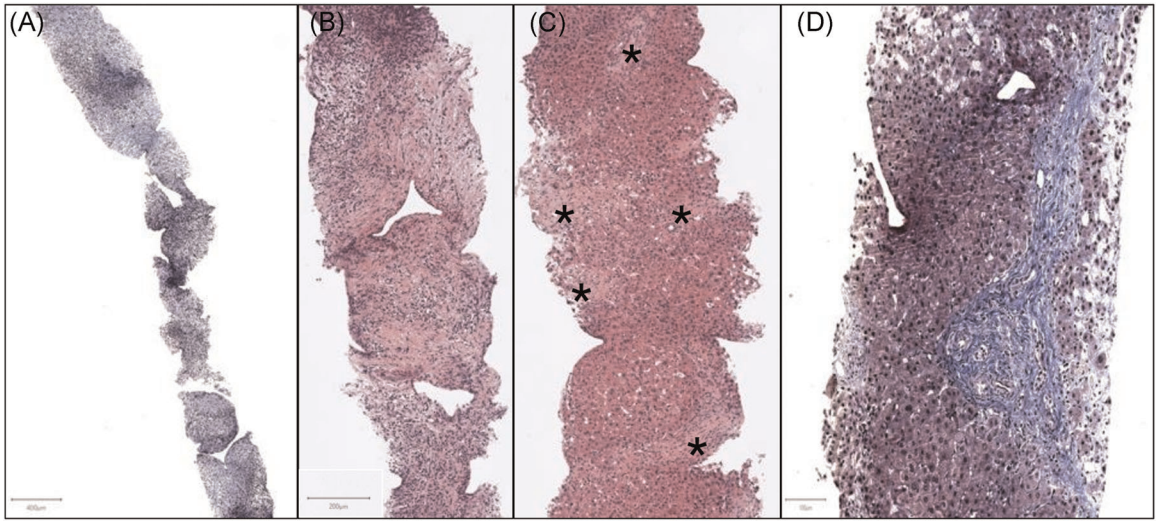

FIGURE 2 Pathology diagnosis. A confluent inflammatory lesion with parenchymal extinction and central fibrosis takes the central part of the biopsy (A, trichrome stain). The inflammatory infiltrate is mainly composed of small lymphocytes, macrophages, and plasma cells with few eosinophils and siderophages (B, hematoxylin and eosin). The portal spaces (*) at the periphery of the lesions show fibrosis, loss of portal venules, and ductal/ductular reaction; the triads are abnormally closer due to hepatocyte loss and atrophy (C, hematoxylin and eosin). Massson trichrome stain highlights architectural changes and fibrosis in the portal–periportal region (D). No features suggestive of venous outflow impairment or coagulative ischemic necrosis were observed

gallbladder vasculitis,[7–9] have been described in affecting hepatic circulation.[10]

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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