Acute Liver Infarct with a Superimposed Liver Abscess as a Consequence of Hypercoagulable State in a Patient with COVID-19 without Respiratory Manifestations

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COVID-19 infection has been associated, particularly in severely ill patients requiring hospitalization, with a hypercoagulable state. The case presented herein was a 66-year-old man with SARS-CoV-2 infection who did not have any respiratory symptoms. He presented with the following clinical manifestations: portal vein and hepatic artery thrombosis, liver infarction, and a superimposed abscess of the liver. In this case, early detection and the administration of anticoagulants and antibiotics led to a significant improvement within weeks of the diagnosis. We encourage physicians to be aware of COVID-19–associated hypercoagulable state and its potential complications, regardless of the acuity of the presentation or the absence of respiratory symptoms. [*P R Health Sci J 2023;42(1):81-84*]

Key words: COVID-19, Hepatic infarction, Liver abscess, Portal vein, Thrombosis

COVID-19 infection's symptoms are varied and most commonly range from a mild upper respiratory tract infection to severe viral pneumonia leading to multiorgan failure and death. Significant evidence has emerged about thromboembolic complications, most of them associated with poor outcomes (1–4). Evolving theories about excessive inflammatory response, endothelial dysfunction, hypoxia, and vascular stasis have risen as possible explanations for the hypercoagulable state (5); in addition, several reports have described deep venous thrombosis and pulmonary embolism as the most common presentations (1,2,3). Only 7 cases have reported acute portal vein thrombosis (PVT) (6). We present the first known case of acute PVT with evidence of a liver infarction leading to a superimposed infection and subsequent hepatic abscess in the setting of COVID-19.

Case Report

A 66-year-old man with hypertension, hyperlipidemia, and type 2 diabetes mellitus presented to the emergency department (ED) in San Juan, Puerto Rico, with right-sided flank pain. A non-contrast computed tomography (CT) scan showed a 0.5-cm calculus in the right kidney, without hydronephrosis or perinephric stranding. In view of a recent trip off the island of Puerto Rico 2 weeks prior, a COVID polymerase chain reaction test was done, the results of which were positive. The bloodwork showed mild anemia and elevated liver enzymes—all new findings (Table 1). He was discharged with a diagnosis of nephrolithiasis and COVID-19 with instructions to self-quarantine.

Ten days after the initial visit, the patient returned to the ED complaining of fever, night sweats, generalized malaise, unintentional weight loss, and epigastric abdominal pain. He denied respiratory symptoms, nausea, vomiting, diarrhea, melena, hematochezia, or jaundice. A physical examination showed an oriented man in no distress and with clear lungs. The abdominal examination was benign. His bloodwork showed neutrophilic leukocytosis, reactive thrombocytosis, normocytic normochromic anemia, elevation of the liver enzymes, and elevation of inflammatory markers (Table 1). An abdominal ultrasound revealed acute PVT.

He was admitted to our COVID-19 unit and started on vancomycin, piperacillin/tazobactam, and enoxaparin. The antibiotic treatment resulted in the resolution of the patient's fever and night sweats by day 2 of admission. A CT scan of the chest showed no pulmonary consolidation or ground-glass opacities. An abdominopelvic contrast CT scan confirmed the presence of a PVT involving the main, right, and left portal veins, without evidence of collateral vessels and consistent with an acute thrombosis. A wedge-shaped area of hypoenhancement involving segment 4 and the anterior

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The authors have no conflict of interest to disclose.

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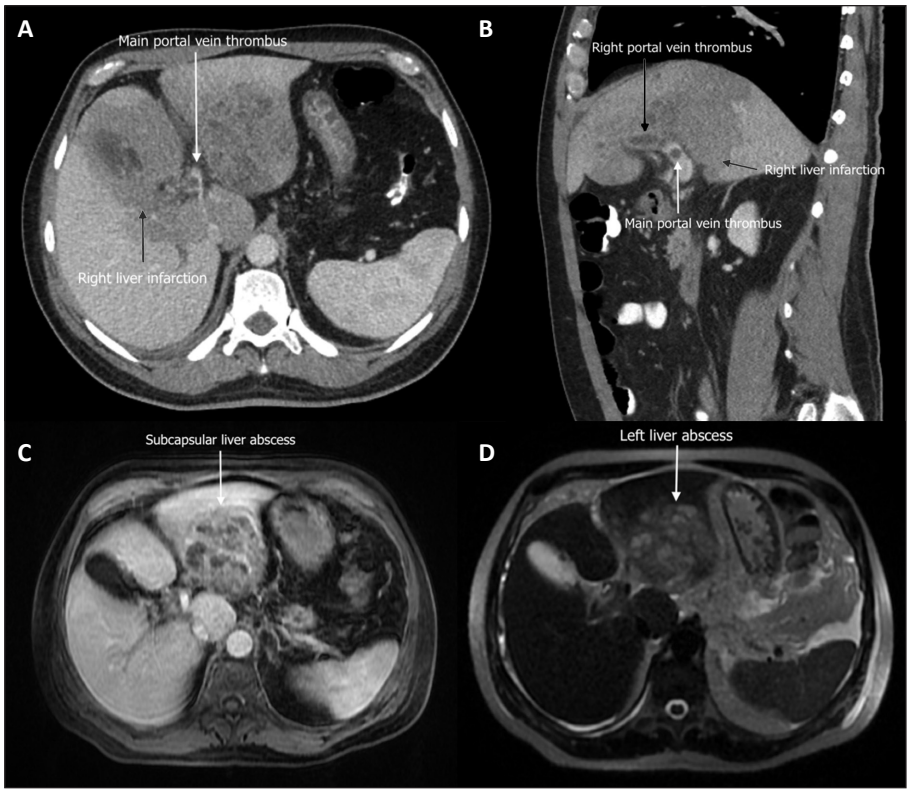

Figure 1. Abdominal CT scan in transverse view (A) and sagittal view (B). Main portal vein thrombus (white arrow) with a wedge-shaped area of hypoenhancement and altered perfusion involving the left liver and anterior right liver and compatible with infarction (grey arrow). T1-weighted (C) and T2-weighted (D) abdominal MRI in transverse view with evidence of a large multiseptated, mass-like lesion in the left liver lobe and compatible with a subcapsular liver abscess.

right liver portion was visualized, suggestive of a large liver infarct. It was accompanied by a superimposed, ill-defined hypoattenuating mass lesion within the left liver lobe suggestive of a liver abscess. No other foci of infection were identified (Figure 1a and 1b). Contrast magnetic resonance imaging showed a multiseptated liver abscess within the lateral segment of the left liver lobe and a PVT associated with a large infarction involving the anterior segment of the right lobe and the medial and lateral segments of the left lobe (Figure 1c and 1d). No signs of portal hypertension were seen. After 6 days of broad-spectrum antibiotics, his leukocytosis resolved and his inflammatory markers improved. His liver enzymes normalized, but his alkaline phosphatase remained elevated (Table 1). Blood and urine cultures were negative; his stool was negative for ova and parasites; an IgG enzyme-linked immunosorbent assay was negative for Entamoeba histolytica; and a viral hepatitis panel was negative. His workup pointed towards inflammation as the culprit of anemia. On day 7, antibiotics were de-escalated to ciprofloxacin and metronidazole. On day 12, the patient was discharged to complete 4 weeks of antibiotics with oral ciprofloxacin and metronidazole and 6 months of anticoagulant therapy with enoxaparin.

The patient denied further fever, night sweats, chills, or abdominal pain on a follow-up appointment 22 days after discharge. A follow-up contrast CT scan revealed unchanged left and right PVT, the development of cavernous transformation of the porta hepatis (compatible with the development of collateral vessels in the setting of a chronic occlusion) and resolution of the previously observed left subcapsular hepatic lobe abscess. (Figure 2).

Table 1. Laboratory tests at the first visit to the emergency department (ED), second visit to the ED (10 days later), first week of admission, and 109 days after discharge

Variable (unit)	First visit to the ED	Second visit to the ED	1 week after admission	109 days after discharge	Reference
White blood cells (10^{-3}/µl)	7.0	20.7	11.4	5.1	4.3–9.3
Neutrophils (%)	72.3	89	79	55.4	34–74
Lymphocytes (%)	18.2	3.9	10	31.4	17–48
Hemoglobin (g/dL)	12.2	10.3	9.6	13.5	12.6–17.8
MCV (fL)	84.1	83.8	85.1	85.5	81–102
Hematocrit (%)	36.5	31.1	29.8	42.3	37.9–54.5
Platelets (10^{-3}/µl)	221	638	576	137	155–371
PT (seconds)	-	16.4	15.4	30	11.8–15.0
PTT (seconds)	-	32.9	30.6	-	22.4–38.3
INR	-	1.28	1.19	2.79	1.5–3.0
ALT (U/L)	113	132	45	42	0–45
AST (U/L)	95	93	29	37	0–40
LDH (U/L)	-	352	-	-	60–200
ALP (U/L)	142	298	245	133	30–115
Total bilirubin (mg/dL)	0.5	0.9	0.5	0.3	0.2–1.3
Sed rate (mm/1hr)	-	116	114	-	0–15
CRP-HS (mg/L)	-	>300	182.1	-	≤5.0
Ferritin (ng/mL)	-	1,774	977.2	-	30–400
D-dimer (µg/mL)	-	4.45	-	-	≤0.48
IL-6 (pg/mL)	-	-	82.44	-	2.5–7

-: laboratory data not available; MCV: mean corpuscular volume; PT: prothrombin time; PTT: partial thromboplastin time; INR: international normalized ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; CRP-HS: high sensitivity C-reactive protein; IL-6: interleukin-6

Discussion

Current World Health Organization, American College of Chest Physicians, and National Institutes of Health guidelines recommend the use of low-dose anticoagulants for prophylaxis of venous thromboembolism (VTE) in hospitalized patients with COVID-19, regardless of the disease severity (7,8,9,10). The use of therapeutic doses of anticoagulation for this purpose remains controversial. Experts affirm that although anecdotal reports suggest that there is a higher incidence of VTE in critically ill patients with COVID-19, there is an insufficient number of randomized control trials to determine the optimal dose of anticoagulation in these patients (9). Although observational studies have shown a lower mortality associated with anticoagulation in patients with COVID-19 in whom D-dimer levels reach up to 6 times the upper limit of normal (11), others have shown that such an elevation in D-dimer levels also correlates with a major risk of bleeding and mortality (12). Thus, experts have suggested that the higher risk of bleeding outweighs the benefits of therapeutic anticoagulation, even in the absence of completed trials.

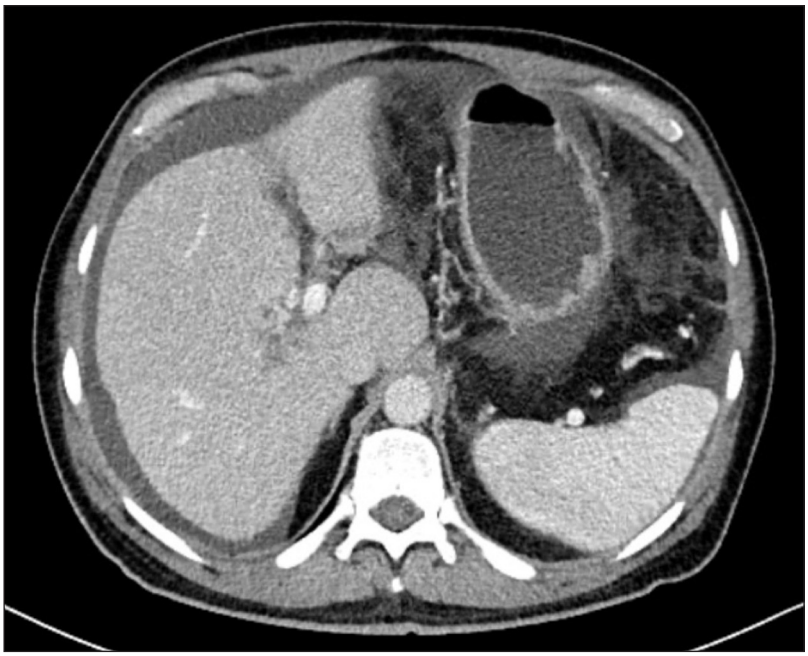

Figure 2. Follow-up abdominal CT scan, triple phase, in transverse view with improved hypoattenuating area of the left liver lobe, with cavernous transformation and patent main portal vein.

As witnessed in this case, the presentation of a PVT can be non-specific, with symptoms overlapping the gastrointestinal manifestations of COVID-19 (13,14). In this case, local and systemic causes of acute PVT, such as hepatocellular carcinoma, liver cirrhosis, intra-abdominal and pelvic inflammation, and infection, were absent, and there was no history of coagulopathies or prior thrombotic events. Thus, we must postulate that the hypercoagulable state associated with COVID-19 led to thrombosis of the portal vein and branches of the hepatic artery, eventually leading to the patient's clinical presentation and ultimate complications.

Early anticoagulation in PVT has been shown to be the most significant independent factor for promoting the recanalization of a thrombosed vessel, which is crucial to the prevention of portal hypertension and mesenteric ischemia (14). In this case, early therapeutic doses of anticoagulation led to a significant improvement, which was evidenced by cavernous transformation and stable PVT in a follow-up abdominopelvic CT scan 3 weeks after the patient's admission. Based on our findings, we counsel physicians to be aware that patients with SARS-CoV-2 infection can debut with thromboembolic phenomena as the only clinical manifestation of COVID-19. Prompt recognition can help physicians to direct appropriate therapy earlier in the development of these complications, which can have a significant impact on the outcomes and prognoses of such patients. While the final data are published, we encourage physicians to be aware of the hypercoagulable state in COVID-19 and have a low index of suspicion for systemic thromboembolic manifestations of the disease, even in patients without respiratory symptoms.

Resumen

La infección por el COVID-19 se ha asociado, particularmente en pacientes severamente enfermos que requieren hospitalización, con un estado hipercoagulable. En el siguiente reporte, presentamos el caso de un hombre de 66 años de edad con infección por SARS-CoV-2 sin síntomas respiratorios, que debutó con trombosis de la vena porta y ramas de la arteria hepática. Esto causó infarto hepático y un absceso sobreimpuesto como su única manifestación clínica del COVID-19. En este caso, la detección temprana y la administración de anticoagulantes y antibióticos condujeron a una mejora significativa a pocas semanas del diagnóstico. Este escrito tiene como fin concientizar a la comunidad médica sobre las complicaciones asociadas al estado hipercoagulable del COVID-19, independientemente de la agudeza de la presentación o de la ausencia de síntomas respiratorios.

Acknowledgment

The contents of this manuscript do not represent the views of the VA Caribbean Healthcare System, the Department of Veterans Affairs, or the United States Government.

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