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Atypical COVID–19 presentation with Budd-Chiari syndrome leading to an outbreak in the emergency department

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ABSTRACT

We described a case report of a 50 years-old-woman admitted to the emergency department with abdominal pain associated with febrile hepatosplenomegaly with the final diagnosis of suprahepatic vein thrombosis secondary to COVID-19. Initially, this patient stayed out of a private room because of this atypical presentation and caused a COVID-19 outbreak in the emergency department.

1. Introduction

The SARS-CoV-2 virus infection causes a broad spectrum of presentation, ranging from asymptomatic or mild upper airway symptoms to acute respiratory failure [1]. The recognition of a vascular involvement associated with a hypercoagulable state allows atypical clinical presentation with any vascular territory involvement [2,3]. We describe an atypical presentation of coronavirus disease 2019 (COVID-19) with Budd-Chiari syndrome due to hepatic vein thrombosis without respiratory symptoms during the early phase that causes an emergency department outbreak because this patient was not initially placed into a private room.

2. Case report

A 50-years-old woman was admitted to the emergency department with severe right upper quadrant abdominal pain for 6 days associated with nausea and vomiting. She observed both jaundice and unmeasured fever 2 days before hospitalization. The patient has a previous asthma diagnosis and uses an inhalator corticoid. She denied pregnancy, oral contraceptive use, and alcohol consumption. On physical examination, we observed jaundice and pain during palpation of the right upper quadrant abdominal. Her vital signals on presentation showed a blood pressure of 110/70 mmHg, a pulse of 95 beats per minute, respiratory rate of 20 cycles per minute, and arterial oxygen saturation of 96% on room air. Initially, she denied any respiratory symptoms. The general laboratory tests are shown in Table 1. Abdominal ultrasound showed hepatomegaly and enlarged spleen, without biliary tract obstruction and ascites. Firstly, the differential diagnosis was performed among some infectious or autoimmune diseases. However, the laboratory tests for infectious and autoimmune diseases were negative. Table 1 On the third day of hospitalization, the patient started with a sore throat and a runny nose. At this moment, she was placed into a private room, and the real time polymerase chain ration (RT-PCR) of the oropharyngeal swab for the SARS-CoV-2 virus was positive. At this time, a second abdominal ultrasound imaging showed an echogenic material inside the left suprahepatic vein compatible with partial thrombosis of this vein. Fig. 1 Computed tomography of the thorax and abdomen and magnetic resonance imaging (MRI) of the abdomen confirmed the presence of partial thrombosis of the left suprahepatic vein, without any pulmonary commitment. Fig. 1 The patient received anticoagulation with rivaroxaban 20 mg/day. Laboratory evaluation for thrombophilia was performed, and the tests did not confirm this diagnosis, except for the presence of low levels of anti-cardiolipin IgM. Table 1 The patient presented a good clinical evolution with normalization of the liver biochemical tests. A new MRI was performed 3 months later and showed complete resolution of the left suprahepatic vein thrombosis, and the repeated anti-cardiolipin IgM was negative. This patient's clinical presentation was compatible with a Budd-Chiari syndrome, and since no other predisposing factor was found, we believe that this event was related to SARS-CoV-2 virus infection. Initially, because of this atypical presentation, this patient stayed out of a private room. After this, twenty healthcare workers of the emergency department were confirmed for SARS-CoV-2 virus infection in the next 2 weeks. We hypothesized that this patient could have been the index case of this hospital outbreak.

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Table 1
Laboratory tests.

	Value	Normal range
General		
Bilirubin, direct (mg/dl)	7.90	0.40
Bilirubin, total (mg/dl)	9.20	0.80–1.20
Aspartate aminotransferase-AST (U/L)	180	32
Alanine aminotransferase-ALT (U/L)	140	31
Alkaline phosphatase (U/L)	523	65–300
Gamma-glutamyl transpeptidade-GGT (U/L)	240	11–50
Serum albumin (g/dl)	2.70	3.5–4.8
Prothrombin time (INR)	1.07	<1.30
APTT (ratio)	0.99	<1.26
Thrombin time (ratio)	0.98	<1.20
Alpha-fetoprotein (ng/ml)	6.41	<8.10
Hemoglobin (g/dl)	9.80	12.00–15.50
Leucocytos (/mm^3)	10,100	3500–10,500
Platelets (/mm^3)	42,000	150,000–350,000
Reactive C-protein (mg/dl)	22.66	0.50
Creatinine (mg/dl)	0.59	0.70–1.60
Infectious diseases		
SARS-CoV-2 RT-PCR	Positive	Negative
Dengue virus serology (IgM)	Negative	Negative
Yellow fever RT-PCR	Negative	Negative
Leptospirosis serology (IgM)	0.2	<1.1
Hepatitis B surface antigen (HBsAg)	Negative	Negative
Anti-hepatitis C virus antibody (HCV)	Negative	Negative
Anti-hepatitis A serology IgM	Negative	Negative
Epstein-Barr virus seroloy IgM	0.08	1.00
Cytomegalovirus serology IgM	0.11	1.00
HIV serology test	<0.05	1.00
Autoimmune diseases		
Anti-nuclear antibodies (ANA)	Negative	Negative
Anti-neutrophil cytoplasmic antibodies (ANCA)	Negative	Negative
Anti-mitochondrial antibodies (AMA)	Negative	Negative
Anti-smooth muscle antibodies (SMA)	Negative	Negative
Anti-liver/kidney microssomal-1 antibodies (LKM-1)	Negative	Negative
Hypercoagulable states		
Anti-cardiolipin IgG (pg/mL)	5.40	<10
Anti-cardiolipin IgM (pg/mL)	7.80	<7
Anti- β2-glycoprotein IgG (U/mL)	<9.40	<20
Anti- β2-glycoprotein IgM(U/mL)	10.40	<20
Protein C (%)	148	70–130
Protein S (%)	150	55–123
Lupus anticoagulant (LA)	Negative	Negative
Factor V Leiden gene mutation	Negative	Negative
Prothrombin gene mutation	Negative	Negative
Antithrombin III, (%)	116	80–120
Janus kinase 2 (JAK2) gene mutation	Negative	Negative

INR: international normalized ratio; APTT: activated partial thromboplastin time; RT-PCR: real time polymerase chain reaction.

3. Discussion

COVID-19 is associated with a hypercoagulable state [2]. High rates of thrombotic events have been described in these patients, mainly of deep vein thrombosis and pulmonary embolism, even in patients receiving thromboprophylaxis. Fox et al. [4] reported a high cumulative incidence of thrombotic complications (49%) in critically ill patients with COVID-19.

Thrombotic complications in a variety of vascular territories have been described during the COVID-19 pandemic [5]. We describe a Budd-Chiari syndrome case due to suprahepatic vein thrombosis during acute SARS-CoV-2 virus infection without respiratory symptoms during the early phase. In the medical literature, there are accumulative reports of portal vein thrombosis probably secondary to SARS-CoV-2 virus infection [6-8]. There are descriptions of splanchnic and mesenteric vein thrombosis in these patients too [9-11].

Portal and suprahepatic vein thrombosis usually occurs in patients with cirrhosis, malignancy, or thrombophilia [12]. Some intra-abdominal infections such as pancreatitis, cholecystitis, diverticulitis can also predispose this occurrence. In our case, the patient underwent an extensive investigation, and we did not find another cause for this thrombotic presentation beyond the acute SARS-CoV-2 virus infection. Only low titers of anti-cardiolipin IgM antibody were observed during the acute phase; however, this repeated test was negative after 3 months. These findings ruled out antiphospholipid syndrome diagnosis. There are descriptions of transitorily anti-cardiolipin antibodies positivity in SARS-CoV-2 infected patients [13].

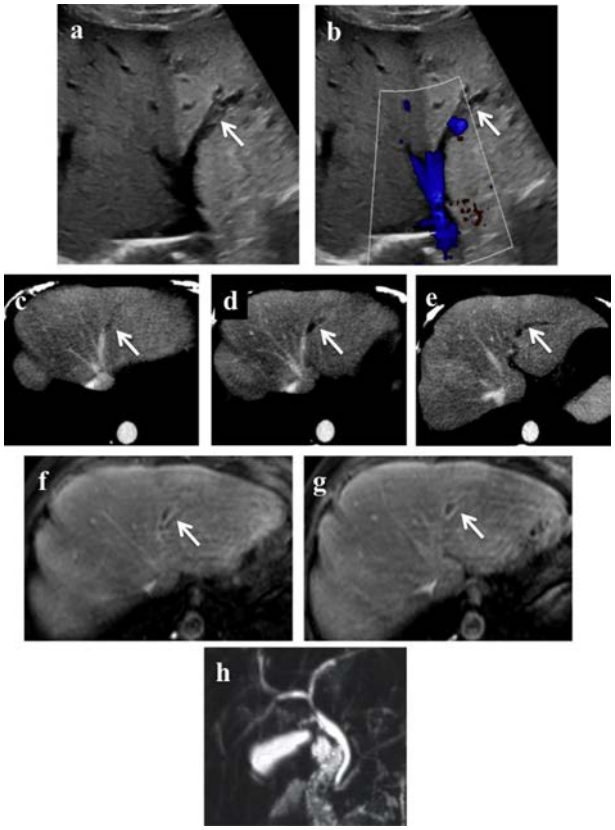

Fig. 1. Axial ultrasound scans without (a) and with color Doppler (b) demonstrate echogenic material (white arrows) inside the left supra-hepatic vein compatible with partial thrombosis. Axial post-contrast scans of computed tomography (c, d, e) and magnetic resonance imaging (f, g) confirm the finding of thrombosis of the left supra-hepatic vein (white arrows). Magnetic resonance cholangiography shows a regular anatomical aspect of the bile ducts, gallbladder, and pancreatic duct (h).

These events associated with COVID-19 seem to be related to *in situ* thrombosis caused by multifaceted mechanisms included activated coagulation, endotheliopathy, up-regulated innate and adaptive immunity, and the activated complement system [2].

Post-mortem liver biopsies from 48 patients who died from severe pulmonary COVID-19 disease confirm that liver failure is not a main concern and this organ is not the target of significant inflammatory damage. On the other hand, the findings are highly suggestive for marked derangement of intrahepatic blood vessel network secondary to systemic changes induced by the virus [14].

The emergency physician needs to recognize these atypical manifestations and place patients with similar presentations immediately into the private room while waiting for RT- PCR for SARS-CoV-2 virus results to avoid emergency department outbreaks.

4. Conclusion

Thrombosis of an abdominal vessel (portal vein, suprahepatic vein, mesenteric vein, *etc.*) should be remembered as a differential diagnosis

in patients with undefined abdominal pain and elevated liver biochemical tests in the department emergency during COVID-19 pandemic.

Declaration of competing interest

The authors declare no conflict of interest.

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