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CASE REPORT
Cardiac imaging

Bi-atrial thrombosis in a patient with SARS-CoV-2 infection: a case report

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Background Coronavirus disease 2019 (COVID-19) is a rapidly spreading pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a multisystemic disease associated with micro- and macrovascular thrombo-embolic complications, including intracardiac thrombosis, which has not been previously reported in the literature.

Case summary We report a case of a 68-year-old woman with COVID-19 admitted to our intensive care unit with acute respiratory distress, undifferentiated shock, hyperkalaemia, acute kidney injury, and coagulopathy. She received crystalloid infusion, broad-spectrum antibiotics, hydroxychloroquine, insulin–dextrose, calcium gluconate, sodium bicarbonate, and i.v. vasopressors. Continuous renal replacement therapy (CRRT) was started for refractory hyperkalaemia and metabolic acidosis. Transthoracic echocardiogram obtained for concern of pulmonary embolism found bi-atrial thrombosis with normal bi-ventricular dimensions and function. Systemic anticoagulation was provided, but this was stopped soon afterwards due to worsening coagulopathy and bleeding. Despite intensive measures and supportive therapy, the patient developed worsening hypoxia, refractory shock, and multiorgan failure. After discussion of goals of care with her family, a decision was made to initiate hospice care. The patient died within 72 h of hospital admission.

Discussion Infection with SARS-CoV-2 is a multisystemic disease that primarily affects the lungs, but also predisposes to rare thrombo-embolic phenomena such as intracardiac thrombosis.

Keywords COVID-19 • Bi-atrial thrombosis • Coagulopathy • Hypercoagulable state • Case report

Learning points

- Patients with SARS-CoV-2 infection frequently have hallmark features of disseminated intravascular coagulation; however, they also express a hypercoagulable state that puts them at risk of severe thrombo-embolic phenomena.
- Patients with COVID-19 can develop intracardiac thrombosis even with a normal heart anatomy and function.

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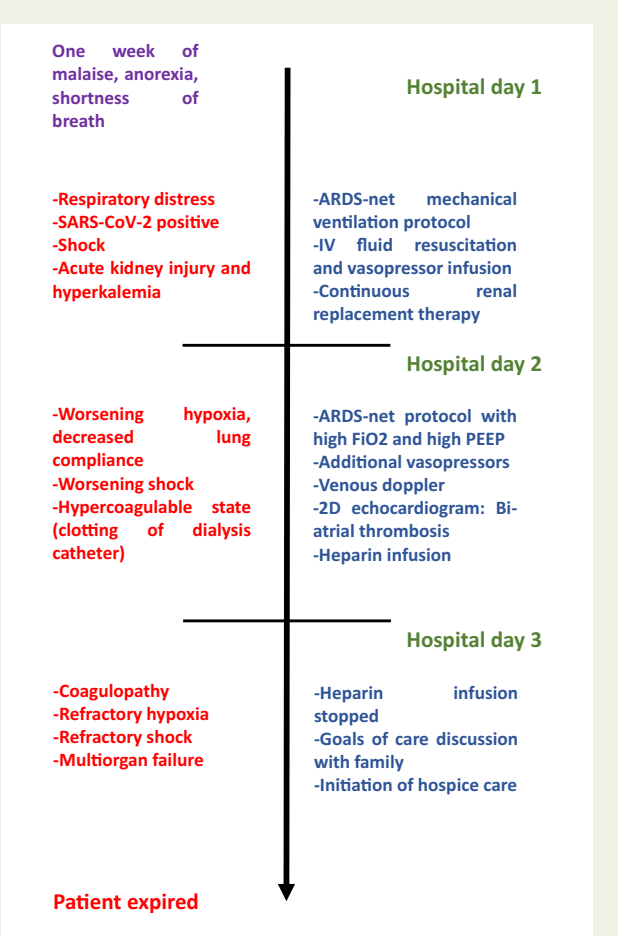
Introduction

Coronavirus disease 2019 (COVID-19) is a rapidly spreading pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] It is a multisystemic disease that has been associated with hypercoagulability and increased risk of thrombo-embolic complications. Micro- and macrovascular thrombosis including occlusion of pulmonary capillaries, limb ischaemia, and venous thromboembolism have been described, predominantly in critically ill patients.[4,5] Further understanding of the pathophysiological mechanisms driving coagulopathic changes is imperative for the development of effective anticoagulation strategies that take into consideration the haemorrhagic events also reported with SARS-CoV-2 infection.

Timeline



Case presentation

A 68-year-old female with insulin-dependent diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) 3-A, and schizophrenia presented with 1 week of malaise, anorexia, and shortness of breath. She was assisted by emergency medical services and was intubated in the field for severe respiratory distress and oxygen saturation of 64% while breathing on ambient air. On arrival to the emergency department, her blood pressure was 82/43 mmHg, heart rate 58 b.p.m., temperature 34.8°C, and oxygen saturation 100% while intubated on 100% FiO_2. She had dry mucous membranes, bilateral wet crackles, and delayed capillary refill of 4 s on physical exam.

Pertinent laboratory results showed hypernatraemia, hyperkalaemia, azotaemia, mixed metabolic acidosis, elevated troponin, elevated inflammatory markers, anaemia, leukocytosis, neutrophilia, prolonged coagulation times, and elevated D-dimer (*Table 1*). ECG identified widened QRS complexes with peaked T waves. Chest X-ray showed diffuse airspace opacities (*Figure 1A*). Nasopharyngeal swab PCR was negative for influenza and respiratory syncytial virus. SARS-CoV-2 PCR was positive.

Initial management included resuscitation with crystalloid infusion, broad-spectrum antibiotics, hydroxychloroquine, insulin–dextrose, calcium gluconate, sodium bicarbonate, and i.v. norepinephrine. The acute respiratory distress syndrome (ARDS) mechanical ventilation protocol was implemented and continuous renal replacement therapy (CRRT) was started for acute kidney injury (AKI) and refractory hyperkalaemia. Despite these interventions, the patient developed worsening haemodynamic instability, worsening hypoxia, and progressive worsening of pulmonary airspace opacities (*Figure 1B*) with elevated plateau and driving pressures. Additional vasopressors were required with only mild improvement of blood pressure. Blood, urine, and sputum cultures obtained on presentation were negative after 48 h.

Clotting of the dialysis catheter was identified multiple times. Venous Doppler of the lower extremities was obtained with normal results. A 2-D echocardiogram was performed for concern of haemodynamically significant pulmonary embolism. Moderate left ventricular (LV) hypertrophy with a small and underfilled LV cavity was found; bi-ventricular systolic and diastolic function as well as valvular anatomy were normal. Two large thrombi with one in each atrium were incidentally identified (*Figure 2*). The patient was started on a heparin infusion which was stopped soon afterwards due to marked thrombocytopenia, rapid elevation of her international normalized ratio (INR), bleeding around catheter insertion sites, and coffee-ground material seen in the orogastric tube. Unfortunately, the patient developed worsening coagulopathy, refractory hypoxia, severe lactic acidaemia, refractory shock, and multiorgan failure. After discussion of goals of care with her family, a decision was made to initiate hospice care and the patient died within 72 h of hospital admission.

Discussion

COVID-19 is a rapidly spreading pandemic caused by SARS-CoV-2. The virus invades the host cells by binding to the angiotensin-converting enzyme 2 (ACE-2) receptor, which is largely found in the lung parenchyma, the heart, and intestine. Pulmonary symptoms are the most common presentation of the disease; however, new evidence suggests a multisystemic involvement with activation of innate inflammatory pathways and an increased release of interleukins leading to the development of cytokine release syndrome (CRS).[1–3]

Table 1 Laboratory results on the day of presentation and at 48 h post-admission

Laboratory parameter	Normal reference range	Day 1	Day 3
Sodium	136–146 mmol/L	153	150
Potassium	3.6–5.1 mmol/L	8.4	5.8
Chloride	98–107 mmol/L	122	99
Bicarbonate	23–31 mmol/L	6	19
Urea	10–20 mg/dL	108	71
Creatinine	0.6–1.0 mg/dL	5.8	2.7
Calcium	8.4–10 mg/dL	9.4	6.7
Anion gap	7–16 mmol/L	25	32
Phosphorus	2.3–4.7 mmol/L	6.9	5.1
Alkaline phosphatase	40–150 IU/L	102	88
Total bilirubin	0.2–1.2 mg/dL	0.2	0.2
Direct bilirubin	0.1–0.5 mg/dL	0.1	0.2
Albumin	3.4–4.8 gm/dL	3.1	1.4
ALT	0–55 IU/L	20	21
AST	5–34 IU/L	22	43
Troponin	0–0.03 ng/mL	0.10	–
LDH	125–220 IU/L	–	333
Ferritin	5–204 ng/mL	551	3281
CRP	0–5 mg/L	207.8	–
WBC	4–11 $\times$ 10^3/μL	12.3	15.3
Haemoglobin	12–16 g/dL	9.6	8.2
Platelet	140–400 $\times$ 10^3/μL	300	44
Neutrophil absolute	1.7–8.4$\times$ 10^3/μL	10	11
Lymphocyte absolute	0.4–4.2$\times$ 10^3/μL	1.5	3.4
PT	11.8–14.3 s	18.1	32.6
INR	0.9–1.1	1.4	3.0
Fibrinogen	191–491 mg/Dl	–	604
D-dimer	270–490 ng/mL	>25 000*	8820
Arterial pH	7.35–7.45	6.96	7.50
PCO_2	34–45 mmHg	32	40
PaO_2	79–87 mmHg	276	74
Lactic acid	0.5–2.0 mmol/L	9	>13.7*

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; WBC, white blood cell count; PT, prothrombin time; INR, international normalized ratio. * Levels above the reference range

Coagulation disorders are frequently reported among COVID-19 patients and have been associated with increased disease severity and worse outcomes.[4–6] The pathophysiological mechanisms are still unclear, but virus-induced endothelial dysfunction and immune activation may be implicated. Exaggerated cytokine release and use of steroids in critically ill patients may increase blood viscosity, while central venous catheterization and invasive procedures may serve as a nidus for clot formation. Additionally, the presence of diabetes, hypertension, coronary artery disease, peripheral artery disease, prior ischaemic stroke or venous thrombo-embolism (VTE), and immobilization may also increase the potential risk of VTE in COVID-19 patients.[7]

Our report describes an elderly woman with cardiovascular risk factors, but no known history of cardiovascular disease or VTE who presented with SARS-CoV-2 infection symptoms and was admitted to the intensive care unit (ICU) with acute hypoxic respiratory failure and AKI. Inflammatory and coagulopathy markers including ferritin, C-reactive protein (CRP), lactate dehydrogenase (LDH), prothrombin time (PT)/INR, and D-dimer were all elevated, indicating a high risk for development of ARDS and subsequent mortality.[5,8,9] Her course rapidly progressed, with worsening haemodynamic instability, which precluded pronation as part of the ARDS management strategy. Elevated D-dimer, elevated troponin, hypoxia, and shock raised concern for pulmonary embolism; however, the presence of AKI limited our ability to perform a CT pulmonary angiography. Instead, venous Doppler of the lower extremities and 2-D echocardiogram were obtained, with incidental findings of bi-atrial thrombosis.

Pathologies that favour intracardiac blood stasis such as dilated cardiomyopathy, acute myocardial infarction, LV aneurysm, valve disease/prosthesis, and atrial fibrillation (AF) are associated with increased risk of thrombi, but, unlike our patient, these frequently involve the left atrial appendage or the LV wall.[10,11] Thrombi in the body of the right atria can also develop with or without involvement of the appendages and are sometimes identified as migrating clots

from the systemic venous system. Endocardial disease (e.g. hypereosinophilic heart disease or endomyocardial fibrosis), collagen vascular disease (e.g. amyloid), and hypercoagulable states, as in our patient, are also important risk factors for intracardiac thrombosis.[12]

Although epidemiological data about the incidence of VTE in COVID-19 are still lacking, it is clear in clinical practice that critically ill patients with the disease are hypercoagulable. Similar to our case, reports have appeared about patients frequently clotting off venous access devices such as dialysis catheters and triple lumen central venous catheters. These observations come along with laboratory findings including thrombocytopenia, high D-dimer, and hyperfibrinogenaemia, which has been associated with resistance to heparin products.[13] Critically ill patients with COVID-19 frequently have hallmark features that meet the International Society on Thrombosis and Hemostasis (ISTH) criteria for disseminated intravascular coagulation (DIC);[14] however, the mechanisms underlying those coagulation abnormalities may represent a mix between increased coagulability and consumption of clotting factors.[13,15]

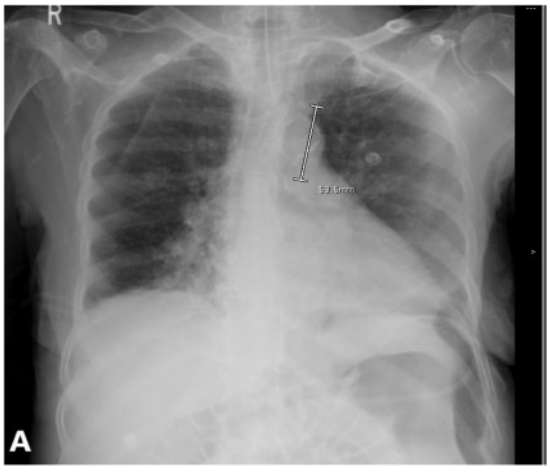


Figure 1 Chest X-ray on presentation to the emergency department (*A*) and at 24 h post-admission (*B*). Note worsening infiltrates more pronounced in the right and left lower lung lobes.

Conclusion

To date, there is no report regarding intracardiac thrombosis in COVID-19 patients with normal heart anatomy and function, but, as described in other studies, this probably reflects a complex mechanism of systemic inflammation, endothelial injury, increased blood viscosity due to hyperproduction of clotting factors, and consumption coagulopathy. Treatment with systemic anticoagulation in our patient resulted in objective evidence of bleeding. Effective and timely anticoagulation strategies that balance the haemorrhagic risks in these patients are needed.

Lead author biography

Ricardo Torres attended Medical School at the Universidad de El Salvador, Facultad de Medicina, San Salvador, El Salvador. He is currently an internal medicine resident at Albert Einstein Medical Center, Philadelphia, PA, USA.

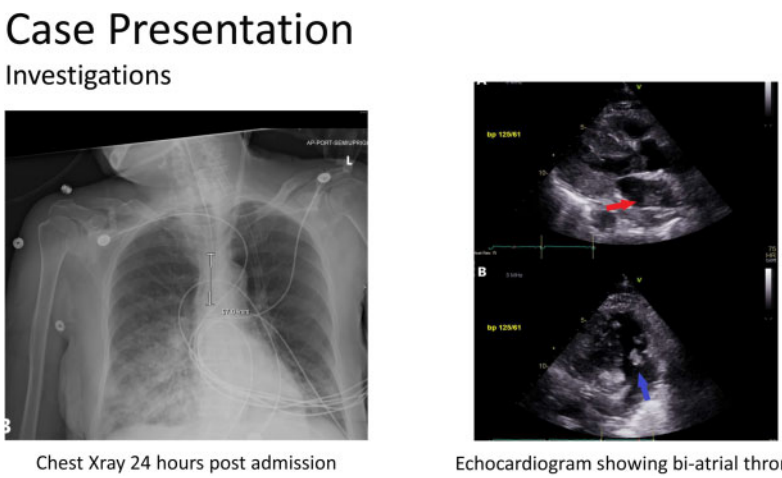


Figure 2 Transthoracic echocardiogram showing a thrombus in the lateral wall of the left atrium (red arrow in *A*) and thrombus without an identifiable stem projecting into the right ventricle through the tricuspid valve (blue arrow in *B*).

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient's next-of-kin in line with COPE guidance.

Conflict of interest: none declared.

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