Bilateral renal infarction with COVID-19 pneumonia: a case report

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Abstract
Acute renal infarction is a rare and often underdiagnosed condition with estimated incidence of 0.5–1.5%. Coronavirus disease 2019 (COVID-19) has been shown to cause a hypercoagulable state in patients leading to arterial and venous thromboembolism. Renal infarction as a consequence of COVID-associated coagulopathy has been reported, sometimes resulting in acute kidney injury. Most of the patients so far reported had other existing comorbidities and risk factors that compounded the risk of precipitating an infarction. Here, we present a 37-year-old, the youngest patient reported so far, with no pre-existing comorbidities or risk factors, who developed bilateral renal infarction with COVID-19 pneumonia. The patient was treated with anticoagulation for renal infarction and discharged on apixaban. Anticoagulation is an important part of current treatment strategies for COVID-19 pneumonia and should extend beyond the acute phase of the disease to prevent long-term sequelae, especially in young patients.

INTRODUCTION
A new type of coronavirus, the SARS CoV-2, was identified in January 2020, which caused coronavirus disease 2019 (COVID-19) [1]. Though primarily shown to cause interstitial pneumonia worsening to acute respiratory distress syndrome, COVID-19 has also been reported to be precipitate a hypercoagulable state leading to arterial and venous thromboembolism [2]. Although pulmonary thromboembolism has been most commonly encountered, there have been cases where patients had cerebral, myocardial and abdominal visceral infarction. Very few cases with renal infarction have been reported to date, with most of them having multiple comorbidities and risk factors. Here, we present the youngest patient so far reported, with no comorbidities, who developed COVID-19 pneumonia with bilateral renal infarction.

CASE REPORT
A 37-year-old male presented to the emergency department with complaints of bilateral flank and suprapubic pain since 2 days. The pain was sudden in onset, continuous, 5/10 in severity and aggravated with coughing and deep breathing. His past medical history was significant for hospitalization for urinary tract infection with development of ureteral strictures requiring stents 5 years ago. There was no family history of cancer or blood disorders. At presentation, his vitals were normal with blood pressure of 100/75 mm Hg. On examination, he was non-toxic, alert, oriented and in pain. Physical examination was significant for bilateral costovertebral angle tenderness. Imaging showed bilateral pneumonia on X-ray and computed tomography (CT) of chest. Contrast enhanced CT of abdomen showed brisk excretion of contrast, no hydronephrosis and bilateral wedge-shaped non-enhancing areas in the renal parenchyma consistent with infarcts (Fig. 1a and b).

Labs were significant for positive COVID-19 infection on reverse transcription-polymerase chain reaction of nasal swab and negative for IgG antibodies. Serum creatinine, blood urea nitrogen (BUN) and urinalysis were normal. Hypercoagulability workup including platelet count, prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), Factor V levels and mutation analysis, antineutrophil cytoplasmic antibodies (ANCA), complement, anti-double-stranded DNA, cardioplin antibody, beta-2-microglobulin and serum homocysteine were all normal (Table 1). Renal arterial and venous duplex showed preserved renal perfusion and no significant stenosis in the visualized segments of renal arteries.

Patient was admitted for COVID-19 pneumonia and bilateral renal infarction. He was started on dexamethasone (6 mg) daily, Lovenox (70 mg) twice daily...
Figure 1. (a) Linear wedge-shaped infarct in left kidney (yellow arrow) on contrast enhanced CT. (b) Linear wedge-shaped infarct in right kidney (red arrow) on contrast enhanced CT.

| Metabolic profile          | At admission | Day 3 | Day 4 | At discharge |
|----------------------------|--------------|-------|-------|--------------|
| Weight in kg               | 68           |       |       |              |
| BMI (kg/m²)                | 25           |       |       |              |
| Creatinine (mg/dl)         | 0.9          | 0.7   | 0.5   | 0.5          |
| BUN (mg/dl)                | 13           | 8     | 7     | 12           |
| AST (IU/L)                 | 384          | 192   | 67    | 86           |
| ALT (IU/L)                 | 414          | 309   | 188   | 221          |
| ALP (IU/L)                 | 90           | 103   | 86    | 90           |
| Bilirubin (mg/dl)          | 0.5          | 0.5   | 0.4   | 0.5          |
| Albumin (g/dl)             | 3.7          | 3.4   | 3.2   | 3.2          |
| Cholesterol (mg/dl)        | 69           |       |       |              |
| LDL (mg/dl)                | 25           |       |       |              |
| LDH (IU/L)                 | 365          |       |       |              |
| HbA1c (%)                  | 5.3          |       |       |              |
| CRP (mg/dl)                | 9.482 (0–0.9)|      |       |              |
| Ferritin (ng/ml)           | 1990 (3.1–110.9)| |       |              |

| Coagulation profile        |              |       |       |              |
| D-dimer (mg/ml)            | 226          |       |       |              |
| PT (sec)                   | 13.3         |       |       |              |
| PTT (sec)                  | 34.6         |       |       |              |
| INR                        | 1.2          |       |       |              |
| Platelet count (per μl)    | 150 000      | 171 000| 194 000| 235 000      |
| Factor V                   | No mutation  |       |       |              |
| Fibrinogen (mg/dl)         | 505 (217–521)|      |       |              |

| Serology                   |              |       |       |              |
| ANCA                       | Negative     |       |       |              |
| C3 (mg/dl)                 | 108 (81–157) |       |       |              |
| C4 (mg/dl)                 | 34 (13–39)   |       |       |              |
| dsDNA (IU/ml)              | <12          |       |       |              |
| Cardiolipin antibodies     | Negative     |       |       |              |
| Homocysteine (μmol/l)      | 9.2 (<15)    |       |       |              |
| Beta-2-microglobulin (mg/l)| 2.1 (0.8–2.2)|       |       |              |

| Urinalysis                 |              |       |       |              |
| Specific Gravity           | 1.040        |       |       |              |
| pH                         | 6            |       |       |              |
| Protein                    | Trace        |       |       |              |
| Hemoglobin                 | Negative     |       |       |              |
| Sugar                      | Negative     |       |       |              |
| Nitrite                    | Negative     |       |       |              |
| Leucocyte Esterase         | Negative     |       |       |              |

LDL: low density lipoprotein; AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase; dsDNA: double-stranded DNA; CRP: C-reactive protein; LDH: lactate dehydrogenase. Normal range values in parentheses.

subcutaneously, IV fluids and supplemental oxygen at 5 liters/min through nasal canula. Because of his deranged liver enzymes, the patient was not considered a candidate for remdesivir. He received 1 unit of convalescent plasma. Pain gradually subsided and patient recovered saturating at 98% on room air at the time of discharge. He was discharged on apixaban (5 mg) daily for renal infarction.
**Table 2.** Summary of cases reported so far with renal infarction and COVID-19 pneumonia

| No. | Study          | Age | Gender | Kidney involved | Thrombus                  | AKI   | Remarks                                     |
|-----|----------------|-----|--------|-----------------|---------------------------|-------|---------------------------------------------|
| 1   | Mukerjee et al.| 71  | Male   | Left            | Left renal artery and ascending aorta | No     | No comorbidities                            |
| 2   | Post et al.    | 62  | Male   | Allograft       | N/A                       | Yes   | HTN, HSP, post-transplant immunosuppression |
| 3   | Anazco et al.  | 58  | Male   | Bilateral      | N/A                       | Yes   | Obesity, untreated DM                       |
| 4   | Ammous et al.  | 41  | Female | Bilateral      | Left renal artery         | No    | HTN, BA. Presented 14 days after COVID and while on LMWH prophylaxis; cardiopulmonary Ab positive |
| 5   | Xu et al.      | 46  | Male   | Transplanted No kidney | N/A                       | Yes   | Kidney pancreatic transplant on Immunosuppression, HTN, Type 1 DM and dyslipidemia; rehospitalization after initial discharge |
| 6   | El Shamy et al.| 60s | Female | Bilateral      | Renal and celiac arteries | Yes   | Afib on apixaban, HTN and HFpEF            |
| 7   | Varner et al.  | 46  | Male   | Right          | Right renal artery        | N/A   | No comorbidities                            |
| 8   | Kundal et al.  | 39  | Female | Right          | Aortic thrombus           | No    | OCP use, PFO, uncontrolled HTN, lupus anticoagulant positive. COVID antibodies present, PCR negative |
| 9   | Mantica et al. | 67  | Female | Right          | N/A                       | No    | Lobectomy for lung adenocarcinoma on chemotherapy |
| 10  | Lushina et al. | 84  | Male   | Left           | Aortic arch               | N/A   | HTN, Afib with RVR at presentation         |
| 11  | Ramanathan et al.| 54 | Male   | Bilateral     | N/A                       | No    | Obese, post COVID discharge                |
| 12  | Tascon et al.  | 56  | Male   | Left           | Left renal artery         | No    | DM, dyslipidemia and diverticulosis        |
| 13  | Imoto et al.   | 64  | Male   | Bilateral     | N/A                       | No    | Gastric and duodenal ulcer, MCA, splenic infarctions |
| 14  | Besutti et al. | 54  | Male   | Right          | Renal artery              | N/A   | BA, Ulcerative colitis, Smoker             |

HTN: hypertension; HSP: Henoch-Schonlein glomerulonephritis; OSA: obstructive sleep apnea; DM: diabetes mellitus; BA: bronchial asthma; Afib: atrial fibrillation; HFpEF: heart failure with preserved ejection fraction; OCP: oral contraceptive pill; PFO: patent foramen ovale; RVR: rapid ventricular response; MCA: middle cerebral artery; MVR: mitral valve replacement; N/A: not available.

**DISCUSSION**

The incidence of renal infarction is 0.5–1.5% [3]. The most common causes of renal infarction are trauma, right atrial embolism from cardiac thrombus, dissection and iatrogenic complications of endovascular procedures [3]. Hypercoagulable states constitute a less common cause of renal infarctions reported. Infection with SARS CoV-2 has been shown to be associated with thromboembolic phenomena due to hypercoagulable state of the blood [2]. Various theories have been proposed regarding the pathophysiology of thrombi formation in the lungs of acutely ill COVID-19 patients including dysregulation of hemostasis, inflammation induced cytokine storm driven activation of endothelium and platelets, hypoxic vasoconstriction and direct viral effects [4]. The role of antiphospholipid antibodies has also been elucidated as a causative factor for COVID-19 associated coagulopathy [5].

COVID-19 has been shown to be frequently causing venous thromboembolism with arterial thrombus formation constituting a minor yet dangerous complication [6]. Hypercoagulability with elevated D-dimer, prolonged PT, APTT, thrombocytopenia and presence of fibrin degradation products have been shown to portend a poor prognosis in COVID-19 patients [7]. Although pulmonary thromboembolism and deep venous thrombosis are more commonly encountered, cerebral, myocardial and infarctions of the abdominal viscera have also been reported [6].

Renal infarction has also been reported with and without the presence of arterial thrombi in the renal vasculature. Thrombotic microangiopathy has also been described as a cause for acute kidney injury (AKI), after studying the post-mortem findings in COVID-19 patients [8]. Very few cases have been reported where patients developed renal infarction with COVID-19 pneumonia. Most of the patients had underlying comorbidities or factors, which added to the risk of developing infarction along with the hypercoagulability due to COVID-19. Bilateral renal infarction has been seen in less than five cases (Table 2). Our patient is the youngest that has so far been reported, with renal infarction and COVID-19 pneumonia. He did not have any comorbidities or risk factors that could have contributed to him developing bilateral renal infarction. Cardioembolic origin was ruled out with normal findings on 2D echocardiogram. Serology ruled out hypercoagulable states like Factor V mutation, protein C and S deficiency and autoimmune causes. There was no family history of bleeding or coagulation disorders, and his coagulation profile was...
also found to be normal. In the light of all these findings, COVID-19 coagulopathy as the cause of his renal infarction is a strong possibility.

Although there have been recommendations on the prophylactic early use of anticoagulation with low molecular weight heparin (LMWH) in COVID-19 patients, especially in an intensive care unit setting, there is no consensus on the duration of anticoagulation treatment needed after resolution of the acute phase [9]. Few case reports have suggested the persistence of hypercoagulable state in COVID-19 patients even after the resolution of acute phase (Table 2). This requires constant monitoring and prolonged anticoagulation especially in young patients such as ours, who have no contraindication for prolonged anticoagulation. Further studies are required to delineate the duration of anticoagulation needed in COVID-19 patients to prevent thromboembolic phenomena.

Hypercoagulability due to COVID-19 is a challenging complication that needs to be addressed not only with early institution of anticoagulation therapy but also to be controlled even after resolution of acute phase. Extended duration of anticoagulation will help in preventing thrombi formation as a long-term sequela of the disease.

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