

A return to normal kidney function in a Caucasian male after COVID-19 induced dialysis-requiring kidney failure

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Case Report

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Abstract

Background: Coronavirus disease 2019 also known as COVID-19 has been recognized by WHO as a global pandemic and has spread to most of the world. The disease has a multitude of clinical presentations, and especially the development of acute kidney injury has been associated with increased mortality.

Case Presentation: A 71-year old Caucasian male was admitted with fever and dyspnea to the emergency department. His medical history included type 2 diabetes and hypertension. Blood tests showed a normal kidney function before admission with a creatinine of 0,8 mg/dL. Clinical examination, blood tests and Chest X-ray suggested COVID-19. At admission the diagnose COVID-19 was confirmed, fluid therapy was commenced and Angiotensin-converting enzyme therapy discontinued. The patients was intubated due to respiratory failures and transferred to the intensive care ward where he developed acute anuric kidney failure and was started in continuous renal replacement therapy. After 6 days of dialysis treatment his kidney function slowly started to improve, and he was discharged after 26 days of admission. 42 days after admission his creatinine was measured to 1.3 mg/dL

Conclusion: We present the rare case of a Caucasian male, who not only survived COVID-19 induced kidney failure that required continuous renal replacement therapy, but returned to almost baseline creatinine. We discuss the role of Angiotensin-converting enzyme inhibitor treatment in COVID-19 and the potential pathophysiological mechanism surrounding AKI in COVID-19 patients in literature, and connect it to our case report.

Background

In December 2019 Wuhan city in the Hubei Province of China became the center of an outbreak of pneumonia of an unknown cause. In January 2020 scientist had identified the cause to be a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). WHO later designated the pneumonia caused by the virus, as coronavirus disease 2019 (COVID-19).

Patients with COVID-19 present with a multitude of clinical presentations. Acute kidney injury and the need for renal replacement therapy has been associated with increased morbidity and mortality. In a retrospective study of COVID-19 patients from Wuhan, all patients (n=10) requiring renal replacement therapy died.

With this case report we present, to our knowledge, the first case of a Caucasian patient tested positive for COVID-19, who, despite developing acute kidney injury and requiring renal replacement therapy, survived and even returned to baseline creatinine.

Case Presentation

71 year old Caucasian man was admitted to the hospital with fever (>39°C) and malaise for 10 days. The patient presented with fatigue, malaise and dyspnea. He mentioned having had diarrhea about a week prior to admission.

The patient's medical history included: Type 2 diabetes mellitus and hypertension. Concurrent medications at admission: Metformin (Biguanide) 1 g x 2 daily , **Vildagliptin** 50 mg x 2 daily, Ace inhibitor Enalapril 20 mg x 1 and Calcium channel blocker Amlodipine 10 mg x 1 daily).

Exposures: 14 days prior to the admission, the patient had been on a ski trip to Norway. After returning home the patient was informed that one member of the traveling party was tested positive for COVID-19.

On admission, the patient appeared ill but responded relevant to questions. He was awake and alert.

The patient presented with a blood pressure of 149/73 mmHg, a temperature of 38.9 °C and a pulse of 106. The peripheral blood oxygen saturation was 84% without oxygen and 91% on 5 liters oxygen by nasal cannula. The electrocardiogram was unremarkable, apart from sinus tachycardia.

Auscultation of the lungs revealed decreased breathing sounds, predominantly on the right side, while cardiac auscultation was normal and without murmurs. There was no sign of edema in the lower extremities. Abdominal examination was normal.

Laboratory results at the time of admission can be seen in **Table 1**:

Table 1		
Blood test and Units	Patients lab results	Reference value
Hb g/dL	13.1	12-16
Leucocytes 10 ⁹ /L	5,86	4-11
CRP mg/L	139	<10
Trombocytes 10 ³ /L	202	150-450
Neutrofilocytes 10 ⁹ /L	4,97	2.0-7.5
Lymfocytes 10 ⁹ /L	0,55	1.0-4.5
Monocytes 10 ⁹ /L	0,29	0.3-0.9
Basofilocytes 10 ⁹ /L	0,01	0.0-0.30
Eosinophils 10 ⁹ /L	0,00	0.04-0.4
Albumine g/L	31	35-50
Potassium mmol/L	4,9	3.5-4.6
Creatinine mg/dL	1.12	0.5-1.10
Blood Urea g/dL	24.92	7.0-25
eGFR	66	>60
Sodium mmol/L	135	135-146
D-dimer mg/L	1,34	0.7
INR	0,98	0.9-1.2
ALAT IU/L	34	5-35
Amylase IU/L	40	25-120
Billirubine µmol/L	6	3-17
Alkaline Phosphatase IU/L	67	30-130
LDH IU/L	432	140-280
Blood glucose mmol/L	21,5	5,5-10

The chest x-ray showed ground glass infiltrates characteristic for COVID-19.

Urinary dipstick: +3 glucose, +2 blood +2 protein and negative for Leucocytes, ketones and nitrite.

The patient was given Piperacillin/tazobactam intravenously and given 2 liters of i.v. fluid.

The patient was tested for COVID-19 with oral swap and isolated.

Enalapril, Vildagliptin and Metformin were paused shortly after arrival at the emergency ward.

8 hours after admission the patient's respiration worsened and the patient was sedated, intubated and transferred to the intensive care unit (ICU). During this transfer, the patients test for COVID-19 came back positive.

After admission to the ICU, the patients kidney function slowly deteriorated (Table 2), with diminishing urine production. Furosemide infusion was initiated (increasing to 120 mg / day) and 5 days into the admission, continuous renal replacement therapy was started.

Development of the kidney function and urine output can be seen in **Table 2**.

Table 2								
Days since admission	2 months before	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	
Creat mg/dL	0.88	1.12	1.63	2.40	3.42	4.16	4.67	
Blood urea g/dL	x	24.92	28.56	33.32	40.6	53.21	62.45	
Urine Output(mL)	x	x	1620L	1410	1700	800	500	
Note:							CRRT Started	

Continuous renal replacement therapy (CRRT) specifications:

Bloodflow:130 ml/min,

PBP flow with Regiocit: 1300 ml/h

Dialysate with Biphosyl:1300 ml/h

Postreplacement fluid with Phoxilium: 400 ml/h

Fluid removal 100-200 ml /hour

Filter: ST150 Prismaflex

The Patient had no urine production on day 6, and was kept in a negative fluid balance the next couple of days.

On Day 9 the patient had increasing diuresis and the CRRT fluid removal was stopped and the patient was extubated. The patient's clinical status slowly improved and on day 11, the CRRT was paused (6 days CRRT in total), and the patient was given Zaroxilyn 5 mg x 2 and continuous furosemide infusion 40 mg/hour. Slowly but steadily the patient's kidney function and urine production improved.

On day 14 he was discharged from the ICU with a urine production of 3000 mL/day. The renal function improved gradually and 26 days after the admission, the patient was discharged to primary care with a

creatinine of 1.9 mg/dL. 42 days after admission, the patient's creatinine was 1.3 mg/dL

Discussion

Cause of acute kidney injury in COVID-19

The prevalence of acute kidney injury (AKI) in Covid-19 varies from 0.5% (1) of patients to 5% (2) according to Chinese studies. Cheng et al. reported that 43.9% of patients with covid-19 had proteinuria and 26.7% had hematuria on admission (2). AKI was associated with increased morbidity and mortality (2). Zhou et al reported that all of the patients with COVID-19 requiring renal replacement therapy died during their study period (3).

A Chinese study performed postmortem renal biopsies on 6 patients. Severe acute tubular injury, prominent lymphocyte infiltration, detection of viral antigen in tubular epithelial cells, macrophage infiltration and complement C5b-9 deposition were seen (B. Diao, C.H. Wang, R.S. Wang, Z.Q. Feng, Y.J. Tan, H.M. Wang, *et al.*: Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] infection [preprint posted online April 10, 2020]. *medRxiv* doi:10.1101/2020.03.04.20031120). A study investigating 26 postmortem renal biopsies in COVID-19 patients showed also acute proximal tubular injury, but, additionally, peritubular erythrocyte aggregation and glomerular fibrin thrombi with ischemic collapse and signs of pigment casts from rhabdomyolysis (4). To our knowledge, the only alive kidney biopsy performed in Covid-19 patients with AKI was an African American woman with collapsing glomerulonephritis (5).

Ronco et al proposed the following three potential pathways of kidney damage in COVID-19 (6):

1) Cytokine damage or cytokine release syndrome which leads to intra-renal inflammation. Increased vascular permeability, volume depletion and cardiomyopathy leading to cardio-renal syndrome. Cardio-renal syndrome can generally be defined as a pathophysiological disorder of the heart and kidneys, in which dysfunction of one organ may induce dysfunction in the other (7). In the following cases, various cardiac dysfunction lead to compromised circulation and, as a result, to acute kidney injury.

2) Organ crosstalk where high peak airway pressure and intra-abdominal hypertension causes renal compartment syndrome. Alveolar damage leads to renal medullary hypoxia. Cardiomyopathy and myocarditis lead to impaired circulation causing cardio-renal syndrome.

3) Systemic effects: positive fluid balance leading to renal compartment syndrome, third space loss leading to renal hypo-perfusion and endotoxins leading to septic AKI.

Rhabdomyolysis has been described as a feature in both organ crosstalk and systemic effects. CRRT has been suggested as a causal treatment to remove cytokines and treat rhabdomyolysis (6).

Battle et al agree that AKI in COVID-19 patients appears to involve a complex process driven by virus-mediated injury and cytokine storm. However, the authors additionally propose that angiotensin II

pathway activation, dysregulation of complement, hyper-coagulation, and micro-angiopathy play a role (8).

Angiotensin converting enzyme (ACE2) is expressed, among others, in brush border apical membrane of the proximal tubule and podocytes (9). SARS-CoV-2, the strain of coronavirus that causes COVID-19, can bind to renal epithelial cells and injure them. Furthermore, an association between angiotensin II and over-activity of immune and complement pathways and the coagulation systems, have been proposed to play a role in AKI in Covid-19 patients (8).

Elevated d-dimer levels have been shown to correlate with worse outcome pointing towards a hyper-coagulable state in COVID-19 patients which potentially could lead to cortical necrosis (8, 10).

Our patient presented with a d-dimer of 1.34 and only microscopic hematuria. Since cortical necrosis is causing irreversible damage (8), we suppose that, if at all, our patient only suffered from mild cortical necrosis.

Concerns have been raised regarding the safety of inhibitors of the renin-angiotensin-aldosterone system (RAAS) in COVID-19 patients. Recommendations from some medical societies suggest that RAAS inhibitors should be continued since the available data points to the benefits outweighing the risks (11). However NICE guidelines from the 21st of May state that at this stage no conclusion on the role of ACE inhibitors in COVID-19 can be drawn due to the poor quality and subject to bias and confounding of the available data (12). Although mainly based on opinions and observational data, withdrawal or reduction of RAAS inhibition is part of many guidelines for AKI to improve renal perfusion (13). At least in our case report, the cessation of ACE inhibitor had a favorable effect.

We have presented a rare case of full renal recovery after acute, anuric renal failure due to COVID-19. The weakness of the present report is the lack of a renal biopsy, creatinine kinase/myoglobin or reliable quantification of proteinuria. Since the patient was receiving critical care and was later quickly regaining his renal function, a renal biopsy was considered unnecessary in terms of treatment regimen at the time. Our patient was Caucasian and his renal function improved quickly. We, therefore, do not assume collapsing glomerulonephritis as cause for the patient's AKI. We argue that the most plausible cause was acute tubular injury. We cannot rule out rhabdomyolysis as a contributing factor. However, since urine color was described as normal and electrolytes were unaffected, we consider rhabdomyolysis unlikely.

Conclusion

In conclusion, this is the first case report on a COVID-19 patient with AKI receiving acute renal replacement therapy not only surviving, but also, returning to baseline creatinine 42 days after admission. The patient's ACE inhibitor was discontinued and he was treated with CRRT. These factors may have played a role in the restitution of renal function and survival in AKI patients and warrant further investigation.

Declarations

Ethics approval and consent to participate

Not Applicable

Patient perspective

During his discharge, the patient was thankful and felt he had received proper care.

Consent for publication

The patient has given written consent to publish his medical data for this article.

Availability of data and materials

Data sharing not applicable to this article, because no datasets were generated or analyzed during the current study.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

PO wrote the introduction, case presentation and contributed to the discussion and conclusion.

JK's main contribution was in the discussion and conclusion segments.

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