

Persistent Fever in a Kidney Transplant Recipient Diagnosed with COVID-19

ABSTRACT

SARS-CoV-2 disease (COVID-19) presentations range from a mild upper respiratory disease to acute respiratory distress syndrome. At this time, it is unknown whether immunocompromised hosts, specifically kidney transplant patients, are at higher risk of systemic COVID-19 disease. We present the case of a 21-year-old, COVID-19 positive, kidney transplant patient, who was admitted to our ward with fever and dysuria. Initial workup indicated acute kidney injury and pneumonia. During her hospitalization, the patient was treated with IV fluids and antibiotics, resolving the acute kidney injury but not the patient's fever, which remained unexplained.

Introduction

The SARS-CoV-2 pandemic spread to most of the world by 2020. SARS-CoV-2 disease (COVID-19) usually manifests as a respiratory infection with presentation ranging from mild upper respiratory disease to pneumonia, acute respiratory distress syndrome and death. Patients with chronic kidney conditions are at increased risk of severe COVID-19 [1] and COVID-19-related mortality [2]. It remains to be determined whether kidney transplant patients are also at a higher risk of COVID-19 morbidity and mortality.

Organ transplant recipients have frequent contact with the health care system and are therefore potentially more likely to be exposed to the virus. Once exposed, chronic immunosuppression may impair adequate immune response, thereby allowing COVID-19 to develop. Some studies have reported an alarmingly high death rate among solid organ transplant patients afflicted by COVID-19 [3], whereas others suggest that immunosuppression is most likely associated with a better outcome of COVID-19 by mitigating hyperinflammation [4].

Kidney transplant-specific studies have mostly reported high rates of acute kidney injury, respiratory failure and mortality [5-7]. Important questions arise as to the susceptibility, clinical presentation and management of these patients, as well as the expected evolution of the disease and outcome. Here we present the case of a 21-year-old kidney transplant patient who was diagnosed with COVID-19, presented to the ED with fever and was admitted to our ward.

Case report

A 21-year-old woman presented to the emergency department with a fever of up to 40°C and dysuria, which had begun three days prior to her admission. Her past medical history was notable for dysplastic kidney disease for which she had undergone a kidney transplantation from a deceased donor five years prior to her admission. Notably, 4 years after the transplantation she was admitted due to an antibody mediated rejection of the renal allograft treated with IV rituximab, IVIG and plasmapheresis and discharged with an elevated creatinine of 1.2 mg/dL.

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Her immunosuppression regimen included steroids, mycophenolate mofetil and tacrolimus.

At the time of her presentation she denied having a cough, shortness of breath, gastro-intestinal symptoms, chest pain or chills. The patient did not report any contact with SARS2-CoV positive patients. She presented with normal vital signs and the Physical examination was unremarkable. A complete blood count revealed pancytopenia: leukopenia with 3220 / μ L white blood cells, lymphopenia with 740/ μ L lymphocytes, microcytic hypochromic anemia with hemoglobin of 9.2 g/dL and 102,000/ μ L platelets. Kidney function tests indicated acute kidney injury (AKI) with creatinine increased to 2.26 mg/dL, and blood urea nitrogen increased to (BUN) 33.7 mg/dL (Figure 1A-B). Urinalysis revealed proteinuria of 300 mg/dL without leukocytes or nitrites. C-reactive protein (CRP) was elevated at 6.13 mg/dL (Figure 1C). A chest x-ray was done and demonstrated consolidations On the left border of the cardiac silhouette and possibly in the base of the right lung. A SARS-CoV2 PCR swab was positive.

Blood urea nitrogen (BUN, A), creatinine (B) and C-reactive protein (CRP, C) are shown over the course of hospitalization. The upper limit of normal (ULN) is shown in red.

After diagnosing AKI and COVID in a renal transplant patient, admission was recommended. The patients' usual medical treatment was modified as follows: administration of mycophenolate mofetil was stopped and the steroid dosage was increased to a stress dose. Preventive enoxaparin was administered for three days and stopped when the patient reported gross hematuria and mild hemoptysis. Neither hematuria nor hemoptysis reoccurred after administration of enoxaparin was stopped.

During her hospitalization, the patient was treated with IV fluids for presumed prerenal acute kidney

injury. Kidney function tests returned to baseline level following treatment. Unlike the acute kidney injury, the patient's fever did not seem to be resolved. Blood and urine cultures were sterile and urine Legionella Ag was negative. Consolidations on the chest x-ray raised the possibility of community-acquired pneumonia, and therefore empirical ceftriaxone and azithromycin were administered. After a week-long hospitalization, the patient was discharged against medical advice.

Discussion

In spite of loss of follow-up and the fact that the patient was discharged against medical advice, we would like to discuss the management of kidney transplant recipients with COVID-19. As discussed above, these patients are at increased risk of severe COVID-19 and death [6,8,9]. Common presenting symptoms in these patients are fever, dyspnea and cough [6,10], similarly to the general population. Mortality in these patients was associated with older age and a higher respiratory rate at presentation, while high baseline lymphocyte counts and higher eGFR were associated with survival [6].

Supportive care remains the mainstay of therapy as there are no proven antiviral treatments. Administration of immunosuppressive medications is often reduced in dosage or discontinued [10,11], even though consensus on how to adjust immunosuppression is lacking. These decisions are further complicated by the high rates of AKI in kidney transplant recipients hospitalized with COVID-19 [6,12]. Multi-organ failure, cytokine storm and reduced renal perfusion have been proposed as possible mechanisms for AKI in COVID-19 patients. The latter was presumed to be the cause of AKI in the case presented and indeed eGFR improved with administration of IV fluids. Nonetheless, patients with a history of transplant rejection, such as our patient, require particularly careful consideration of any

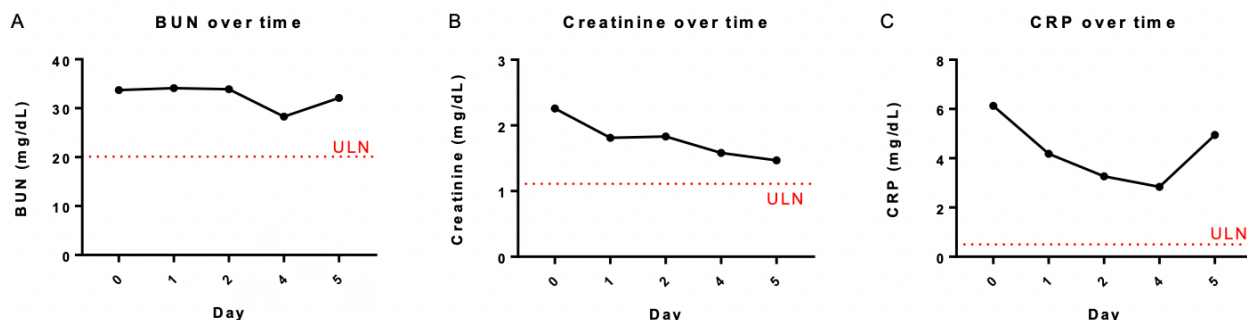


Figure 1: Kidney function tests and C-reactive protein values over the course of hospitalization.

change in immunosuppression.

Persistent fever in COVID-19 kidney transplant patients also presents a challenge, especially as fever in itself in most transplant patients is considered an emergency [13]. Our patient had multiple possible causes of fever, the more probable of which include COVID-19 and urinary tract infection. While the latter are the most common bacterial complications in renal transplant patients [14,15], the infectious and

inflammatory differential diagnosis is wide. To date, work-up recommendations for such patients have not been published. We suggest inpatient management of such cases at least until the prognosis of kidney transplant patients with COVID-19 is better described. Future studies could assist physicians in delineating work-up and initial management of these patients given the wide range of possible causes of fever they present.

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