Central Asian Journal of Nephrology
(eISSN 3105-4145)

Case Report

Acute Tubulointerstitial Nephritis in a Patient Post-Renal Transplantation

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Received: July 31, 2025
Accepted: August 26, 2025

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Abstract:

A 41-year old female patient who underwent kidney transplantation as an outcome of chronic glomerulonephritis came to the hospital with the signs of acute upper respiratory tract infection. As the patient further developed oliguria, peripheral edema, fever, and an increased BP, she was further relocated to the University Medical Center (UMC). Upon admission to UMC, signs of septic shock were detected, and acute transplant rejection was suspected, to exclude which kidney biopsy was performed and stage 3 chronic kidney disease (CKD) in allograft kidney was detected. Antibacterial treatment as well as pulse therapy were performed as patient had septic shock and tubulointerstitial nephritis (TIN).

Keywords: Acute Tubulointerstitial Nephritis; Renal Transplantation; Kidney Transplant Complications; Graft Dysfunction; Transplant Nephropathy; Immunosuppression; Biopsy Findings; Nephrology; Renal Pathology; Case Report

Introduction

Even though kidney transplantation is the definitive treatment for end-stage renal disease, complications such as rejection, infections, and drug toxicity are commonly observed in kidney transplant recipients. Due to the presence of immunosuppression, infections are of particular concern, as it can lead to allograft dysfunction (1, 2). 70% of patients after kidney transplantation are estimated to develop an infection in the first 3 years after transplantation (3). Consequently, infections are the leading cause of admission to the ICU for acute kidney injury (AKI) in kidney transplant patients (1). It is also the second leading cause of mortality in this patient group (3).

Based on the timeline of post-transplantation, the causative pathogens leading to infection differ. For instance, in the first month after the surgery, the source of infection is generally attributed to surgical complications, hospital-acquired infections, and pathogens derived from donors. On other hand, between 1 to 6 months after transplantation, urinary tract infections, the reactivation of latent viruses and opportunistic infections are common. After 6 months, community acquired infections and the delayed presentation of viruses such as the CMV after the discontinuation of prophylaxis need to be considered (4).

Urinary tract infection (UTI), including pyelonephritis, is the most frequent bacterial infection encountered after kidney transplantation (5). Acute graft pyelonephritis is particularly concerning as it is the primary cause of systemic infection in KTRs. Studies have shown that pyelonephritis is especially noted in female patients and may contribute to permanent graft impairment (5).

Another important complication of infection in kidney transplant recipients is tubulointerstitial nephritis (TIN). It is a term that encompasses a group of inflammatory renal diseases that affect the filtration units of the kidney, typically sparing the glomeruli. Medications and infections are among the most common etiologies of tubulointerstitial nephritis. Additionally, TIN

is one of the major causes of renal transplant dysfunction. Allograft dysfunction from TIN is usually due to either bacterial pyelonephritis or BK viral infection. Due to the progression of TIN in a transplanted kidney, its lifespan can be significantly reduced as a consequence of permanent fibrosis (2). Considering the fact that TIN in renal transplant recipients is usually due to viral or bacterial infection, TIN in this patient population usually involves the reduction of immunosuppression, the administration of the antiviral cidofovir, and supportive care in the case of AKI (2).

The following case study presents a kidney transplant recipient with acute kidney injury, pyelonephritis, and sepsis a year post-transplantation. While the patient's biopsy suggested acute tubulointerstitial nephritis, the patient was able to recover fully from her AKI and exhibited improved renal function. This case represents the complexity of managing immunosuppression in infection-triggered TIN in a post-transplant patient.

Case Report

A 41-year old female with a history of chronic glomerulonephritis and subsequent kidney transplantation was admitted to the nephrology unit of University medical centre in a severe condition. The patient was first diagnosed with chronic tubulo-interstitial nephritis in 2018 after an acute viral upper respiratory tract infection, however serum creatinine level was not specified. However, a biopsy of the patient's native kidney was not previously performed before transplantation, thus the morphological diagnosis was not verified. Moreover, this is when the patient started experiencing headaches and a rise in her blood pressure up to 180/100 mm Hg. Her treatment included indapamide for blood pressure control. In January 2020 she was hospitalized to the nephrology department and diagnosed with Chronic nephritic syndrome, CKD stage 3, where she started receiving prednisolone 60 mg per day. Her CKD progressed from Stage 3 to Stage 5 in 2021, after which she started receiving hemodialysis. Such rapid development and progression of CKD to the terminal stage in the patient can be attributed to persistent arterial hypertension rise upto 180/100 mmHG, which was not treated properly due to poor antihypertensive therapy adherence. Also, this period coincides with the COVID pandemic, which can affect and worsen kidney function causing tubulointerstitial damage and can be related to the rapid worsening of patient's condition, however, according to patient's words he did not have COVID-19 history. As a result, in May 2022, she underwent kidney transplantation from a living donor. Post-transplantation, she received maintenance immunosuppression consisting of tacrolimus, mycophenolate mofetil, and prednisone. In December 2022 she received a pulse therapy with methylprednisolone, getting 500 mg on the first day of therapy and 250 mg on the following two days.

Nonetheless, in November 2023, the patient's condition deteriorated after an acute upper respiratory tract infection and she was admitted to a local hospital. She had oliguria, peripheral edema, fever, and an increased BP. Moreover, hydronephrosis of the renal transplant was observed on imaging studies. Consequently, a ureteral stent was inserted to relieve any possible obstruction. Nevertheless, the patient remained in a severe condition. As a result, she was then transferred to UMC hospital for further management.

Upon admission, the patient was in a severe condition. Septic shock was suspected. Her creatinine was 399,2 umol/ (GFR of 12 ml/min) and BUN 18.2 mmol/L. Moreover, the patient had hyponatremia and metabolic acidosis. Hypervolemia was observed as the patient gained 22 kg. Her blood pressure dropped to 90/60 mm Hg. Her hemoglobin was 81.00 g/L, WBCs 23.61x109/L, and platelets 251x109/L. Her CRP was 89.56 mg/L, while procalcitonin constituted 1.03 ng/ml. Her urinalysis demonstrated proteinuria (1.56 g/L) and leukocyturia (500 cells/μl). In addition, her urine culture depicted the presence of a high concentration of Escherichia coli. It was revealed that the patient had chronic hepatitis B infection (HBsAg of 4400COI). Additionally, she had a decrease in the C3 and C4 complement levels, positive IgG and IgM levels toward anti-phospholipid antibodies, and weakly positive IgM antibodies toward β-2-glycoprotein-1. Her ANA panel was negative. After stabilizing the patient, to differentiate between the acute transplantation rejection and the recurrence of the disease, a kidney biopsy was performed. A chronic allograft nephropathy Stage 3 was established.

As the patient had sepsis and acute pyelonephritis, she was given an empirical antibiotic therapy of piperacillin/tazobactam and meropenem. Moreover, given that the patient had hyponatremia, azotemia, hypervolemia, and edema, it was decided to perform ultrafiltration. In addition, to control the patient's hypoalbuminemia and anemia, she received a transfusion of washed red blood cells (RBCs) and recormon 2,000 IU 3 times a week. Furthermore, to induce diuresis, IV furosemide was administered, which was slowly titrated to

subsequent combination of perioral furosemide and spironolactone combination. Further on, as gross hematuria and proteinuria was persisting and taking into account the patient's low complements and positive antibodies toward phospholipids, a pulse therapy with methylprednisolone was initiated starting from 500 mg and lowering to 250 mg. Subsequently, methylprednisolone was given PO with a dosage of 16 mg per day. During the hospitalization, the patient's tacrolimus serum levels reached 9 ng/ml, thus, she was maintained on tacrolimus (4 mg per day) and mycophenolic acid (720 mg per day) as a part of her immunosuppressive regime post-transplant.

Generally, the patient was also provided with a supportive therapy for her gastritis and arterial hypertension. Moreover, hemostatic agents and systemic antifungal therapy were also initiated during the hospitalization.

At the time of discharge, the patient was in a stable clinical condition with no acute complaints. She did not exhibit any signs or symptoms of the infection. Moreover, her blood pressure remained relatively stable at approximately 125/80 mm Hg. Her weight significantly decreased with no peripheral edema noted. Spontaneous voiding was observed with an adequate balance of fluid intake and output. Moreover, her GFR improved up to 56.1 mL/min. On a subsequent planned hospitalization as a part of the patient's regular monitoring in July 2024, her GFR further increased to 76.3 mg/ml. Based on this progression, her diagnosis was revised to chronic allograft nephropathy Stage 2.

Discussion

A 41-year old female post renal transplantation was admitted to the hospital with AKI, pyelonephritis and sepsis for further management.

In this case, the patient's AKI and TIN were most likely the result of a combination of E. coli pyelonephritis, sepsis-induced hypoperfusion, and tacrolimus nephrotoxicity. UTIs, particularly in the setting of ureteral obstruction, remain a critical trigger for graft dysfunction in kidney recipients (5). Elevated tacrolimus levels (9 ng/mL) and increased infection susceptibility may have exacerbated renal injury. Appropriate management, including tacrolimus dose reduction to adjust the immunosuppression, was crucial in reversing AKI in our patient.

It is highly likely that the patient's Escherichia coli-associated pyelonephritis and sepsis resulted in the precipitation of her TIN. Urinary tract infections (UTIs), especially pyelonephritis, are the most common bacterial infections in KTRs and a leading cause of graft dysfunction (3). Additionally, the presence of ureteral obstruction and consequently hydronephrosis likely facilitated ascending infection. Acute interstitial inflammation due to bacterial TIN, compounded by hypoperfusion due to sepsis, might have led to AKI in the patient. It is noteworthy to mention that BK polyomavirus, which is a common viral etiology of post-transplant TIN (3), was not observed in our patient, suggesting the need to exclude other opportunistic pathogens in post-transplant infections.

Furthermore, the patient's immunocompromised state could have rendered her susceptible to infection. The rigorous immunosuppressive regimen in kidney transplant recipients for the prevention of rejection can contribute to a high risk of infection, cancer, and cardiovascular disease (6). Thus, post-transplant patients must be on constant monitoring for dosage adjustment in immunosuppression to prevent the reduction of their allograft function as a consequence of these complications. The elevated concentration of tacrolimus (9 ng/ml) noted in our patient's blood during her hospital stay was indicative of excessive immunosuppression and could have contributed to the progression of her infection. Furthermore, tacrolimus is nephrotoxic (7) and can lead to acute nephropathy which is dose-dependent and reversible. It is triggered by renal vasoconstriction from vasoactive substances and can eventually cause acute kidney injury (AKI) (8). Thus, the adjustment of our patient's immunosuppressive regimen with tacrolimus was an essential step in her management.

Conclusion

This case highlights the significance of strict supervision of patients following renal transplantation. Due to being in an immunosuppressive state, they are susceptible to infections, which can trigger rejection or other renal complications. Here we have presented a case of a post-transplantation patient who regained renal function after acute kidney injury following sepsis and pyelonephritis.

Author Contributions: Conceptualization, Z.K., A,K.; methodology, Z.K., M.M., Z.K., N.N.; writing – original draft preparation, Z.K., B.A.; writing – review and editing, B.A., N.N. All authors have read and agreed to the published version of the manuscript.

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: None.

Ethics approval: Not applicable.

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