ASIDE Case Reports

Case Report

Outcome of Kidney Transplant Patients Following Treatment with Checkpoint Inhibitors: A Case Series

Ahmed I Kamal[1], Mohamed Reyad[2], Menna Keshk[3], Ahmed Daoud[4], Sakshi Vaishnav[5], Munsef Barakat[5], Aurora Salas[5], Mahmoud Nassar[7], Karim Soliman[8]

1-Nephrology Departments, Medical University of South Carolina Charleston, South Carolina, USA
2-Internal Medicine Department, University of Arizona College of Medicine – Phoenix, Phoenix, Arizona, USA
3-Cardiology Department, Faculty of Medicine, Cairo University Cairo, Egypt
4-Nephrology Departments, Medical University of South Carolina Lancaster, South Carolina, USA
5-Nephrology Department, Medical University of South Carolina Charleston, South Carolina, USA
7-Assistant Professor of Medicine, Division of Endocrinology, Larner College of Medicine, University of Vermont, Burlington, Vermont, USA
8-Associate Professor of Medicine, Thomas E. Starzl Institute of Transplantation, University of Pittsburgh/UPMC, Pittsburgh, Pennsylvania, USA

ARTICLE INFO

Article history:
Received 5 Mar. 2025
Received in revised form 21 Jun. 2025
Accepted 1 Jul. 2025
Published 29 Aug. 2025

Keywords:
Immune checkpoint inhibitors
Kidney transplant
Graft rejection
Immunosuppression
Cemiplimab

ABSTRACT

Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment by enhancing immune surveillance against tumors. However, their use in kidney transplant recipients presents a significant challenge due to the risk of immune-mediated graft rejection. This retrospective case series highlights four kidney transplant recipients treated with ICIs for various malignancies, revealing the complex interplay between oncologic outcomes and transplant function. Two of four patients developed severe acute kidney injury (AKI), leading to dialysis-dependent graft loss despite high-dose corticosteroid therapy. One patient exhibited partial renal recovery following transient dialysis. In contrast, another patient maintained stable graft function despite prolonged ICI therapy. Oncologic outcomes varied, with two patients achieving significant tumor regression, while others experienced disease progression. These cases underscore the need for careful immunosuppressive management and close monitoring when administering ICIs in transplant recipients. The findings emphasize the importance of individualized treatment strategies to optimize both cancer control and graft survival.

1. Introduction

Introduction Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment by enhancing the immune system's ability to recognize and destroy tumor cells. Agents such as pembrolizumab, cemiplimab, atezolizumab, and durvalumab work by blocking the programmed death-1/programmed death-ligand 1 (PD-1/PD-L1) pathways, restoring T-cell activity, and overcoming tumor immune evasion. These agents have been particularly effective in treating cancers such as advanced melanoma, non-small cell lung cancer, and cutaneous squamous cell carcinoma (SCC) [1, 2].

However, the use of ICIs in solid organ transplant recipients, particularly kidney transplant recipients, presents a major challenge. These individuals rely on lifelong immunosuppression to prevent graft rejection, which inherently increases their risk of malignancies. The introduction of ICIs can precipitate immune activation and acute allograft rejection, often within weeks of initiation, resulting in graft dysfunction, dialysis dependence, or graft loss [3, 4, 5]. Balancing oncologic control with preservation of the transplanted organ is complex, as immunosuppressive minimization may improve anti-tumor responses but exacerbate rejection risk. Prior studies have reported rates of T-cell-mediated rejection and vascular inflammation following ICI therapy, along with high rates of cancer progression and mortality in this population [3, 5].

This case series aims to explore the outcomes of kidney transplant recipients who were treated with ICIs for various malignancies, providing insights into both the oncologic and renal responses to this emerging class of drugs. By examining the experiences of four patients who underwent ICI therapy, this series highlights the complexities of managing cancer and transplant function simultaneously. The varying responses to ICI therapy underscore the need for individualized treatment strategies, particularly in this vulnerable population. Additionally, the case series illustrates the challenges in optimizing immunosuppressive regimens to mitigate the risk of graft rejection while maximizing the efficacy of cancer therapy. The ongoing challenge of improving both oncologic outcomes and graft survival in transplant recipients requires further research and a multidisciplinary approach to patient care [1, 3]. Our study highlights the urgent need for individualized immunosuppressive strategies and close multidisciplinary coordination to optimize both graft preservation and cancer outcomes in this high-risk population.

* Corresponding author: Mohamed Reyad, Internal Medicine Department, University of Arizona Collage of Medicine - Phoenix, Phoenix, Arizona, USA, Email: mohamedreyad098@gmail.com

Published in collaboration with the American Society for Inclusion, Diversity, and Equity in Healthcare (ASIDE). ISSN (Print) 3066-7224, ISSN (Online) 3066-7232 – see front matter

Citation: Kamal AI, Reyad M, Keshk M, et al. Outcome of Kidney Transplant Patients Following Treatment with Checkpoint Inhibitors: A Case Series. ASIDE Case Reports. 2025;2(1):15-21, doi:10.71079/ASIDE.CR.08292549

2. Case Presentation

2.1. Case 1

A 71-year-old Caucasian male with a history of chronic kidney disease (CKD) secondary to IgA nephropathy underwent a preemptive living donor kidney transplant. The patient received induction therapy with intravenous basiliximab and maintenance immunosuppression consisting of extended-release tacrolimus, mycophenolate mofetil (MMF), and Prednisone. His baseline serum creatinine ranged between 1.3 and 1.5 mg/dL. The post-transplant course was complicated by neutropenia four months after transplantation, necessitating treatment with filgrastim. Given persistent neutropenia, MMF was replaced with everolimus. However, his condition worsened, and he developed low-grade cytomegalovirus (CMV) viremia. Consequently, everolimus was discontinued, and he was maintained on a dual immunosuppressive regimen of tacrolimus and prednisone. Approximately 21 months post-transplant, the patient was diagnosed with poorly differentiated squamous cell carcinoma of the scalp. Initial treatment involved Mohs surgery, followed by local wide excision and salvage surgery with forehead flap reconstruction nine months later. Due to the aggressive nature of his malignancy, cemiplimab therapy was recommended. In preparation for this, tacrolimus was replaced with sirolimus, maintaining target trough levels of 3–5 ng/mL. The patient received the first dose of cemiplimab one week later.

Fifteen days following cemiplimab administration, he presented with severe AKI and nephrotic-range proteinuria. His serum creatinine rose to 10.2 mg/dL (reference range: 0.59–1.04 mg/dL), and urine protein excretion reached 26 g/g (reference range: <150 mg/day). A kidney biopsy revealed widespread cortical coagulative necrosis, moderate tubulitis, and focal severe intimal arteritis. He was treated with an intravenous pulse methylprednisolone, followed by a gradual oral Prednisone taper. Despite aggressive immunosuppression, the patient's renal function failed to recover, resulting in dialysis dependence. One month later, the patient received a second dose of cemiplimab. Following this infusion, he developed gross hematuria, which responded to intravenous pulse methylprednisolone. Given the resolution of hematuria, transplant nephrectomy was deferred. However, oncology specialists advised that nephrectomy should be reconsidered if further cemiplimab therapy was required. To date, the patient has demonstrated significant improvement in his cutaneous malignancy. This case illustrates a severe ICI-associated rejection resulting in graft loss despite pre-emptive adjustment to mammalian target of rapamycin (mTOR) inhibitor-based immunosuppression.

2.2. Case 2

A 66-year-old Caucasian male with end-stage kidney disease secondary to diabetes mellitus and hypertension underwent a deceased donor kidney transplant following 19 months of dialysis. He received induction therapy with anti-thymocyte globulin and was maintained on a triple immunosuppressive regimen of immediate-release tacrolimus, MMF, and Prednisone. His baseline serum creatinine stabilized between 0.8 and 1.0 mg/dL. Approximately two years post-transplant, he was diagnosed with invasive squamous cell carcinoma of the oropharynx and underwent tonsillectomy followed by radiation therapy. However, 18 months later, he experienced cancer recurrence, with biopsy-confirmed invasive SCC of the vallecula and high-grade squamous intraepithelial lesions, along with metastatic spread to the lungs. In response, MMF was discontinued, and three months later, tacrolimus was also withdrawn. The patient subsequently underwent left oropharyngectomy and total laryngectomy, followed by multiple chemotherapy cycles with cisplatin, carboplatin, docetaxel, and cetuximab. Additionally, he received palliative radiation therapy for his lung metastases. Given the progression of his disease, pembrolizumab therapy was initiated. In preparation, he was transitioned to sirolimus. Within 19 days of receiving his second dose of pembrolizumab, he developed oliguric AKI, with serum creatinine rising from a baseline of 0.8 mg/dL to 4.5 mg/dL (reference range: 0.59–1.04 mg/dL). High-dose corticosteroids (500 mg IV methyl prednisone x 3) failed to reverse the AKI, and dialysis was initiated. However, renal recovery was achieved after one month. His current serum creatinine ranges between 1.4 and 1.7 mg/dL. Despite pembrolizumab therapy, his malignancy continued to progress. He is currently being treated with capecitabine for disease control. This case highlights the potential for partial renal recovery following ICI-associated AKI and the limitations of ICI efficacy in aggressive metastatic SCC.

2.3. Case 3

A 65-year-old Caucasian male with end-stage kidney disease secondary to polycystic kidney disease received a prior kidney transplant at the age of 54. Over time, he developed chronic allograft nephropathy, necessitating a second preemptive living donor kidney transplant nine years later. Perioperatively, he was induced with anti-thymocyte globulin and maintained on immediate-release tacrolimus, MMF, and prednisone. His baseline serum creatinine remained stable at 0.9–1.1 mg/dL (reference range: 0.59–1.04 mg/dL). Six months post-transplant, the patient was diagnosed with SCC of the face and underwent multiple surgical excisions, including Mohs surgery. Given the persistent recurrence of skin cancer lesions, MMF was discontinued seven months after the initial SCC diagnosis. Ten months later, everolimus was introduced while maintaining a reduced dose of Tacrolimus. Despite these modifications, the patient continued to experience recurrent SCC lesions. Approximately two years later, cemiplimab was initiated. However, after one year of ICI therapy, he developed poorly differentiated SCC with lymph node involvement and metastasis to the left parotid gland. He subsequently underwent surgical excision of the metastatic lesions, including removal of the left parotid gland, followed by radiation therapy. In response, tacrolimus was discontinued, and the patient was maintained on dual immunosuppression with everolimus and prednisone. Notably, he has experienced no evidence of immune-mediated rejection despite long-term ICI exposure. He continues to receive cemiplimab infusions every three weeks under close monitoring. This case demonstrates that sustained graft function may be possible with mTOR inhibitor-based regimens and close monitoring during prolonged ICI therapy.

2.4. Case 4

A 69-year-old Caucasian male with primary biliary cirrhosis underwent an orthotopic liver transplant. AKI, necessitating dialysis, complicated his postoperative course. Given persistent kidney dysfunction, he subsequently received a deceased donor kidney transplant under the safety net pathway approximately six months later. For induction, he received anti-thymocyte globulin, followed by maintenance immunosuppression with immediate-release tacrolimus, MMF, and prednisone. His baseline serum creatinine stabilized between 0.8 and 1.0 mg/dL (reference range: 0.59–1.04 mg/dL). However, within two months of kidney transplantation, he experienced recurrent urinary tract infections, septic shock, fungemia, AKI, and BK viremia. Due to the high infectious burden, MMF was discontinued. The patient required dialysis for two weeks but eventually regained renal function, with serum creatinine stabilizing at 2.5–3.0 mg/dL. One year post-kidney transplant, he was diagnosed with invasive SCC with lymph node involvement and pulmonary metastases. Despite multiple surgical

Table 1: Clinical Characteristics and Outcomes of Kidney Transplant Recipients Treated with Immune Checkpoint Inhibitors: Case Series

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Birth year	1953	1958	1954	1948
Sex	male	male	male	male
Race	Caucasian	Caucasian	Caucasian	Caucasian
Etiology of kidney disease	IgA nephropathy	DM, HTN	PCKD	CNI nephrotoxicity
Months on dialysis	0	19	0	HD for AKI post-OLT (8 days)
Date of transplant	8/11/2021	12/7/2019	9/16/2019	5/10/2018
Donor age	56	29	54	37
Donor sex	female	male	male	male
Donor type	LUKT	DDKT, DCD, PHS high risk	LUKT	DDKT, DCD, PHS high risk
Induction	Basiliximab	ATG	ATG	ATG
Maintenance immunosuppression	Tacrolimus XR (Envarsus), MMF, Prednisone	Tacrolimus IR (Prograf), MMF, Prednisone	Tacrolimus IR (Prograf), MMF, Prednisone	Tacrolimus IR (Prograf), MMF, Prednisone
Nadir serum creatinine	1.3-1.5 mg/dl	0.8-1 mg/dl	0.9-1.1 mg/dl	0.8-1 mg/dl
Major events post-transplant	Leukopenia, requiring Filgrastim 12/2021-1/2022 MMF switched to Everolimus in 4/2022, but neutropenia worsened Low-grade CMV viremia 4/2022: kept on Tacrolimus, Prednisone only	Tonsillectomy (8/2021)	n/a	OLT (12/12/2017) Multiple episodes of early post-transplant UTI, sepsis, septic shock, fungemia, AKI (required RRT 7/2-17/2018) BK viremia (7/2018-4/2019) BK viruria (6/2018-1/2020)
Cancer diagnosis	Aggressive squamous cell skin CA on the head	Invasive squamous cell CA of the oropharynx with lung metastasis	Poorly differentiated squamous cell skin CA with lymph node involvement and metastasis to the parotid gland	Invasive squamous cell skin CA with lymph node involvement and metastasis to the lungs
Pathology	Acantholytic invasive squamous cell CA, poorly differentiated (5/2023), Dermal deposit of poorly differentiated CA (1/2024)	Tonsillar squamous cell CA (8/2021) Invasive squamous cell CA of the vallecula with background of high-grade squamous intraepithelial lesion (severe dysplasia) (2/2023)	Poorly differentiated squamous cell skin CA	Invasive squamous cell skin CA, poorly differentiated, acantholytic with lymphovascular invasion
Date of diagnosis	5/20/2023	8/2/2021	3/16/2020	6/26/2019
Treatment received for cancer	Mohs surgery Efudex Local wide excision, salvage surgery, local forehead flap reconstruction (2/2024)	Tonsillectomy, surgical excision, radiation therapy (8/2021) L oropharyngectomy, total laryngectomy (5/2023), Cisplatin, Docetaxel, Cetuximab x 1 cycle (7/2023), Cetuximab monotherapy x 2 cycles (7/2023), Carboplatin, Docetaxel, Cetuximab x 3 cycle (11/2023), Palliative radiation of lung nodule (11/2023), Carboplatin, Docetaxel x 4 cycles (1-3/2024) Pembrolizumab monotherapy x 2 cycles (5/2024) Disease progression noted, so switched to Capecitabine (9/2024 onwards)	Multiple surgical excision of skin CA, Mohs surgery; Surgical resection of L parotid gland (9/2024), followed by radiation therapy	Multiple surgical excisions; Mohs surgery; radiation therapy

Table 1 (continued): Clinical Characteristics and Outcomes of Kidney Transplant Recipients Treated with Immune Checkpoint Inhibitors: Case Series

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Immunosuppression changes with malignancy	Switched Tacrolimus to Sirolimus (level 4-5 ng/ml) late 3/2024	MMF discontinued 4/2023 due to CA recurrence FK discontinued 8/2023 Switched to Sirolimus (5/2024) then Everolimus (11/2024)	MMF discontinued (10/2020); Everolimus added to low-dose Tacrolimus (8/2021); Tacrolimus discontinued (9/2024) due to evidence of spread to lymph node and parotid gland	MMF discontinued (3/2018) due to multiple infections and BK viremia
EGFR before Cemiplimab	59 ml/min/1.73 sq.m	105 ml/min/1.73 sq.m	>60 ml/min/1.73 sq.m	25 ml/min/1.73 sq.m
Date of the checkpoint inhibitor	Cemiplimab started on 4/11/2024	Pembrolizumab started on 5/1/2024	Cemiplimab began on 9/21/2023 and given q3weeks	Cemiplimab started on 9/12/2019 and given q3weeks
EGFR after Cemiplimab	21 ml/min/1.73 sq.m	29 ml/min/1.73 sq.m	59 ml/min/1.73 sq.m	25 ml/min/1.73 sq.m
Date of rejection	4/30/2024	5/2024	n/a	n/a
Presentation of AKI	Peak serum crea 10.2 mg/dl Proteinuria 26 g/g			
Kidney transplant biopsy	Widespread coagulative necrosis of the cortex, moderate tubulitis, focal severe intimal arteritis Banff g0, i1, t2, v2, cg0, ci1, ct2, cv3, ah1.5, ptc2, c4d1, mm0, ti2	Not done; presumed rejection	n/a	n/a
DSA	Neg 4/2024	Neg 6/2024	Neg 10/2024	
Treatment received for rejection	Methylprednisolone IV pulse + Prednisone taper	Methylprednisolone IV pulse x 2 cycles	n/a	n/a
Graft outcome	Return to hemodialysis on 4/28/2024	Required HD 6/21-27/2024, then recovered renal function	Excellent graft function	Functioning graft with CKD stage 4

ICI, Immune Checkpoint Inhibitor; AKI, Acute Kidney Injury; DM, Diabetes Mellitus; HTN, Hypertension; PCKD, Polycystic Kidney Disease; CNI, Calcineurin Inhibitor; HD, Hemodialysis; OLT, Orthotopic Liver Transplant; LUKT, Living Unrelated Kidney Transplant; DDKT, Deceased Donor Kidney Transplant; DCD, Donation After Circulatory Death; PHS, Public Health Service; ATG, Anti-Thymocyte Globulin; MMF, Mycophenolate Mofetil; XR, Extended Release; IR, Immediate Release; CMV, Cytomegalovirus; CA, Carcinoma; SCC, Squamous Cell Carcinoma; UTI, Urinary Tract Infection; RRT, Renal Replacement Therapy; EGFR, Estimated Glomerular Filtration Rate; CKD, Chronic Kidney Disease; DSA, Donor-Specific Antibody; BK, BK Virus.

excisions, Mohs surgery, and radiation therapy, his cancer remained progressive. The patient transitioned to palliative care. Approximately one year after his cancer diagnosis, his dermatologist recommended cemiplimab. Following the initiation of cemiplimab, he achieved significant oncologic remission, allowing him to discontinue palliative care. Despite baseline CKD and prior infectious complications, the patient has remained dialysis-free with stable graft function following ICI therapy. This case suggests that ICIs may be cautiously used in patients with impaired graft function and limited therapeutic options, especially when cancer prognosis improves.

3. Discussion

ICIs, including PD-1 inhibitors such as pembrolizumab and cemiplimab, as well as PD-L1 inhibitors like atezolizumab and durvalumab, have significantly advanced cancer treatment by enhancing the immune response against cancer cells [2]. Agents like these inhibit the interactions between PD-1 receptors on immune cells and PD-L1 on neoplastic cells, thereby preventing the tumor's ability to evade the immune system. This enables the immune system to identify and target cancer cells with greater efficacy [6]. However, their use in kidney transplant recipients presents unique challenges due to the risk of immune-mediated graft dysfunction, often manifesting as acute rejection. This case series highlights four kidney transplant recipients who developed different types of malignancies requiring ICI therapy, with varying outcomes in renal function and oncologic response.

3.1. Graft Rejection and Kidney Function Deterioration

The activation of the immune system by ICIs has been observed to provoke acute rejection in transplant recipients, a critical consideration illustrated by the experiences of patients 1 and 2. Patient 1, who was treated with cemiplimab for advanced, poorly differentiated SCC on his scalp, a therapy approved by the FDA in 2018 [7], suffered severe AKI. This was characterized by significant proteinuria and a biopsy showing extensive coagulative necrosis, tubulitis, and intimal arteritis. Despite intensive treatment with high-dose steroids, the patient's condition progressed to the point where dialysis became necessary. Similarly, patient 2 began experiencing oliguric AKI shortly after starting pembrolizumab for recurrent oropharyngeal cancer. Although this patient initially required dialysis, there was a subsequent partial recovery of renal function.

These clinical scenarios are supported by a systematic review and meta-analysis conducted by Wang et al., which underscore the common complications of T-cell-mediated rejection and microvascular inflammation in solid organ transplant recipients undergoing ICI therapy. The review, encompassing over 19,000 patients across 112 trials, noted graft failure rates ranging from 40% to 50%. Furthermore, it highlighted that those fatal toxic effects, though relatively rare, occurred in 0.3% to 1.3% of the patients. The most lethal complications were myocarditis, pneumonitis, hepatitis, and various neurological events, emphasizing the need for vigilant monitoring and prompt intervention [4, 5].

Conversely, patients 3 and 4, who received cemiplimab for advanced CSCC of the head and neck, exhibited stable renal function. Despite ongoing ICI therapy, patient 3 showed no significant renal impairment. Patient 4 maintained graft viability, albeit with suboptimal kidney function exacerbated by previous medical complications such as sepsis and BK viremia. These cases suggest that modulation of immunosuppression, particularly through the use of mTOR inhibitors such as everolimus and sirolimus, may help reduce rejection risks while preserving anti-tumor immunity. Notable in this context is the potential dual benefit of mTOR inhibitors in managing virus-associated post-transplant malignancies and certain cancers like Kaposi sarcoma and mantle cell lymphoma, as highlighted by Fijter et al [8]. Although these inhibitors are primarily cytostatic—halting tumor growth rather than causing regression—recent studies suggest that their use in early conversion to an mTOR inhibitor-based regimen may diminish the cumulative burden of non-melanoma skin cancers.

Despite these promising indications, the evidence remains insufficient to advocate the primary use of mTOR inhibitors as a universal strategy against all malignancies in transplant recipients. The contrasting outcomes between patients underscore the complexity of using ICIs in this vulnerable population and the crucial role of tailored therapeutic strategies based on individual risk assessments and treatment responses [8].

3.2. Oncologic Outcomes and ICIs Efficacy

ICIs have demonstrated variable effectiveness in treating SCC in our cohort. Patient 1 experienced remarkable regression of aggressive, poorly differentiated cutaneous SCC with cemiplimab treatment, although resulting in the loss of graft function. Conversely, patient 2 failed to achieve cancer control with pembrolizumab and subsequently switched to oral capecitabine as a second-line palliative treatment due to disease progression. Patient 3, after one year of Cemiplimab treatment, experienced recurrence and metastasis of poorly differentiated SCC to the left parotid gland, requiring additional salvage radiation and surgical procedures. Patient 4, initially receiving treatment with palliative intent, experienced a remarkable response to cemiplimab, resulting in a significant clinical response as per RECIST criteria. The diverse responses highlight the potential but inconsistent efficacy of ICIs in transplant recipients, affected by factors like previous immunosuppression, the biological features of each type of cancer, and underlying immune regulatory mechanisms [3, 9]. Delyon et al. performed an extensive review and case series about the use of ICIs in solid organ transplant recipients. Their examination of 91 cases, which includes their cohort of five patients, demonstrated that the overall response rates to ICI therapy exhibited considerable variation among distinct cancer types—36% in melanoma, 29% in hepatocellular carcinoma, 14% in non-small cell lung cancer, and 60% in cutaneous squamous cell carcinoma. Nevertheless, the prognosis for transplant recipients undergoing ICI therapy remained unfavorable, with 68% mortality attributed to cancer progression, which was the predominant cause of death, impacting 51% of patients.

In terms of graft survival, kidney transplant recipients demonstrated the highest acute rejection rate at 45%, followed by liver transplant recipients at 36%, and heart transplant recipients at 17%. Rejection rates were significantly elevated in patients administered anti-PD-1/PD-L1 drugs (44%) in contrast to those undergoing anti-CTLA-4 therapy (29%). The median duration from the commencement of immune checkpoint inhibitors to rejection was 22 days, primarily characterized by vascular rejection (Banff Grade 2A or higher) [3]. The significance of managing immunosuppression was emphasized, indicating that mTOR inhibitors may decrease the likelihood of rejection while preserving some tumor response; nevertheless, their overall effectiveness is still ambiguous, as a 35% rejection rate has been noted in patients receiving these inhibitors [3]. Barbir et al. conducted a recent review of immune checkpoint inhibitor medication in kidney transplant recipients, highlighting the associated risks and benefits [1]. Previous investigations suggested elevated rejection rates (40%-50%); however, current

prospective trials have demonstrated reduced rates (0%-12%), indicating that modifications in immunosuppression before initiating ICI therapy could mitigate these concerns. Despite reservations regarding diminished efficacy in immunosuppressed patients, the response rates for advanced skin malignancies in kidney transplant recipients were comparable to those in the non-immunosuppressed cohort. Their findings underscore the necessity of addressing oncologic advantages alongside graft longevity through meticulous immunosuppressive management, taking into consideration patients' preferences and their understanding of the risk of losing their grafted organs. The review promotes a multidisciplinary approach and additional research to refine immunosuppressive methods, boost patient monitoring, and enhance oncologic outcomes while maintaining graft function [1].

3.3. Strategies to Optimize ICI Use in Transplant Recipients

Given the significant rejection risk, optimizing immunosuppression in transplant recipients undergoing ICIs therapy is crucial. An observational study conducted by Dolladille et al. analyzed the safety of ICI rechallenge in cancer patients who had experienced immune-related adverse events (irAEs). The study, based on case reports from the World Health Organization VigiBase, found a 28.8% recurrence rate of irAEs after ICI rechallenge, with colitis, hepatitis, and pneumonitis being the most frequently recurring adverse events. These findings highlight the need for careful immunosuppressive management in transplant recipients receiving ICI therapy [10].

Given the high risk of rejection, strategies to optimize immunosuppression are crucial for success. Some evidence suggests that switching from CNI to mTOR inhibitors could help balance oncologic efficacy with graft preservation. Additionally, early corticosteroid administration, monitoring of donor-specific antibodies (DSAs), and regular assessments of renal function may enhance patient outcomes. Future research should explore personalized immunosuppressive approaches, including biomarkers for predicting rejection risk and strategies to maximize ICI benefits while minimizing complications [10]. Given the significant risk of rejection, optimizing immunosuppression strategies is crucial for effective treatment. Some evidence suggests that switching from CNI to mTOR inhibitors may help balance oncologic efficacy with graft preservation. However, this approach may be limited by adverse events associated with mTOR inhibitors, such as acute rejection, infection, and proteinuria, indicating that conversion therapy may only be suitable for selected patients [11].

According to a Consensus Report with Guideline Statements for Clinical Practice, published in 2023 by Dennis et al., the early administration of corticosteroids or other immunomodulators, combined with close monitoring of DSAs and renal function, may improve patient outcomes. Regular monitoring of DSAs in stable kidney transplant recipients can help identify patients at risk of antibody-mediated rejection and graft failure, allowing for timely interventions. Future research should explore personalized immunosuppressive approaches, including biomarkers for predicting rejection risk and strategies to maximize ICI benefits while minimizing complications [12].

Future research should focus on personalized immunosuppressive approaches, including the use of novel biomarkers to predict rejection risk and strategies to maximize the benefits of ICI therapy while minimizing complications.

3.4. Limitations and Future Directions

This case series is subject to several limitations. First, it represents a small, retrospective sample of four patients from a single center, which limits generalizability and prevents definitive conclusions regarding causality or treatment efficacy. Additionally, the follow-up period varied among cases and was relatively short in some, limiting the assessment of long-term graft survival and oncologic outcomes. Much of the clinical data, including treatment response and symptom burden, relied on retrospective chart review, which may be subject to incomplete documentation and recall bias. Finally, immunosuppressive adjustments were individualized based on clinician judgment, introducing heterogeneity that may affect the interpretation of results. Despite these limitations, the report provides valuable insights into the real-world challenges and outcomes faced by a clinically vulnerable population. Future prospective studies with standardized immunosuppressive protocols and biomarker-driven monitoring are needed to improve outcomes in this vulnerable population.

4. Conclusion

This case series highlights the concurrent issue of treating cancer and preventing graft rejection in kidney transplant recipients undergoing treatment with ICIs. ICI therapy can provide significant oncologic advantages, but it carries a considerable risk of immune-mediated graft malfunction or even rejection. Additional research is required to enhance immunosuppressive approaches, reduce rejection risk, and improve therapeutic outcomes in this particular patient population.

Conflicts of Interest

The authors declare no conflicts of interest related to this manuscript.

Funding Source

No funding was received for this article.

Acknowledgments

None.

Informed consent

Written consent was obtained from the patient to publish this case report.

Large Language Model

No large language models (LLMs) were used in manuscript preparation.

Authors Contribution

All co-authors contributed equally to the conception, drafting, and revision of this article.

Data Availability

Data supporting the findings of this study are not publicly available but can be obtained from the corresponding author upon reasonable request.

References

1. Barbir EB, Abdulmoneim S, Dudek AZ, Kukla A. Immune Checkpoint Inhibitor Therapy for Kidney Transplant Recipients - A Review of Potential Complications and Management Strategies. Transpl Int. 2024;37:13322. [PMID: 39479217, PMCID: PMC11521864, https://doi.org/10.3389/ti.2024.13322].
2. Basudan AM. The Role of Immune Checkpoint Inhibitors in Cancer Therapy. Clin Pract. 2022;13(1):22-40. [PMID: 36648843, PMCID: PMC9844484, https://doi.org/10.3390/clinpract13010003].
3. Delyon J, Zuber J, Dorent R, Poujol-Robert A, Peraldi MN, Anglicheau D, et al. Immune Checkpoint Inhibitors in Transplantation-A Case Series and Comprehensive Review of Current Knowledge. Transplantation. 2021;105(1):67-78. [PMID: 32355121, https://doi.org/10.1097/TP.0000000000003292].
4. Lai HC, Lin JF, Hwang TIS, Liu YF, Yang AH, Wu CK. Programmed Cell Death 1 (PD-1) Inhibitors in Renal Transplant Patients with Advanced Cancer: A Double-Edged Sword? Int J Mol Sci. 2019;20(9). [PMID: 31058839, PMCID: PMC6540260, https://doi.org/10.3390/ijms20092194].
5. Wang DY, Salem JE, Cohen JV, Chandra S, Menzer C, Ye F, et al. Fatal Toxic Effects Associated With Immune Checkpoint Inhibitors: A Systematic Review and Meta-analysis. JAMA Oncol. 2018;4(12):1721-8. [PMID: 30242316, PMCID: PMC6440712, https://doi.org/10.1001/jamaoncol.2018.3923].
6. Iranzo P, Callejo A, Assaf JD, Molina G, Lopez DE, Garcia-Illescas D, et al. Overview of Checkpoint Inhibitors Mechanism of Action: Role of Immune-Related Adverse Events and Their Treatment on Progression of Underlying Cancer. Front Med (Lausanne). 2022;9:875974. [PMID: 35707528, PMCID: PMC9189307, https://doi.org/10.3389/fmed.2022.875974].
7. Research CfDEa. FDA approves cemiplimab-rwlc for metastatic or locally advanced cutaneous squamous cell carcinoma. FDA. 2019.
8. de Fijter JW. Cancer and mTOR Inhibitors in Transplant Recipients. Transplantation. 2017;101(1):45-55. [PMID: 27547865, https://doi.org/10.1097/TP.0000000000001447].
9. Murakami N, Mulvaney P, Danesh M, Abudayyeh A, Diab A, Abdel-Wahab N, et al. A multi-center study on safety and efficacy of immune checkpoint inhibitors in cancer patients with kidney transplant. Kidney Int. 2021;100(1):196-205. [PMID: 33359528, PMCID: PMC8222056, https://doi.org/10.1016/j.kint.2020.12.015].
10. Dolladille C, Ederhy S, Sassier M, Cautela J, Thuny F, Cohen AA, et al. Immune Checkpoint Inhibitor Rechallenge After Immune-Related Adverse Events in Patients With Cancer. JAMA Oncol. 2020;6(6):865-71. [PMID: 32297899, PMCID: PMC7163782, https://doi.org/10.1001/jamaoncol.2020.0726].
11. Zeng J, Zhong Q, Feng X, Li L, Feng S, Fan Y, et al. Conversion From Calcineurin Inhibitors to Mammalian Target of Rapamycin Inhibitors in Kidney Transplant Recipients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Front Immunol. 2021;12:663602. [PMID: 34539621, PMCID: PMC8446650, https://doi.org/10.3389/fimmu.2021.663602].
12. van den Broek DAJ, Meziyerh S, Budde K, Lefaucheur C, Cozzi E, Bertrand D, et al. The Clinical Utility of Post-Transplant Monitoring of Donor-Specific Antibodies in Stable Renal Transplant Recipients: A Consensus Report With Guideline Statements for Clinical Practice. Transpl Int. 2023;36:11321. [PMID: 37560072, PMCID: PMC10408721, https://doi.org/10.3389/ti.2023.11321].