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Case Report

Clear Cell Renal Cell Carcinoma in Allograft kidney 10 years After Living Donor kidney Transplant: A Rare Case Report

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Case Summary

The patient developed end stage renal disease secondary to presumed chronic glomerulonephritis and underwent maintenance hemodialysis in 2010. A year later, at the age of 24 years, he received a living kidney transplant from his sister who was 31 years old. Immunosuppressive therapy was prednisolone, mycophenolate mofetil and cyclosporin. Renalallograftfunction wastable serumcreatinine 0.9mg/dl; then, it rose to 1.7mg/dl in 2020. Ultrasound and computed tomography showed a well-defined space occupying lesion (2×2cm) in the middle cortex of allograft kidney suggestive of renal cell carcinoma. Enucleation was done; the histology was compatible with clear cell renal cell carcinoma. At the time of diagnosis of cancer, the age of patient was 34 years, ten years after transplant. Vigilant post-transplant screening in kidney transplant recipient is important.

Keywords: Clear cell renal cell carcinoma, Allograft kidney, 10 years, Living donor kidney transplant

Introduction

Kidney transplantation is the gold standard for treating patients suffering from end-stage renal disease. It has proven advantages over hemodialysis. While kidney transplantation improves life expectancy and quality of life when compared to that of those on maintenance dialysis, they are having an increased risk of developing cancer. With growing number of kidneys transplants each year, ageing donors, and increasing graft survival, masses in the renal graft become more prevalent in clinical practice. Risk of malignancy following immunosuppressants in recipients with kidney transplant were mentioned in some studies and case reports [1]. One review identified an average time interval of 11.6 years between kidney transplantation and diagnosis of Renal Cell Carcinoma (RCC) with the range of 6 months to 30 years. They highlighted that more than 10 years was a risk for RCC [2]. Regarding the clinical presentation, nearly two third of the kidney transplant recipients with allograft RCC were asymptomatic [3]; the minority presented with hematuria, elevated creatinine, abdominal or graft pain, weight loss, fever, malaise, or hypertension. They pointed out the incidence of asymptomatic allograft RCC among kidney transplant recipients [3]. Therefore, regular screening was important. As of cell type of RCC, the majority were clear cell carcinoma; and it was possibly genetically determined [4]. Dahle et al pointed out the need for research on allograft RCC among kidney transplant recipients including genetic study [5].

Case Presentation

The patient was 37 years old man. He was nonsmoker. He underwent hemodialysis in December 2010. He had history of hypertension for 10 years; and the cause of End Stage Renal Disease (ESRD) was probably due to chronic glomerulonephritis. In 2011, at the age of 24 years, he received a living kidney transplant from his sister who was 31 years old. Both ultrasonogram and CT renal angiogram of donor did not reveal renal pathology in pre-transplant screening of donor. Induction immunosuppressive drugs were not given at the time of transplant surgery. He was on prednisolone, mycophenolate mofetil and cyclosporin as combined immunosuppressants. Post-transplantcoursewasuneventful. Renalallograftfunction was back to normal at one month after transplant; and, serumcreatinine was 0.9mg/dl.

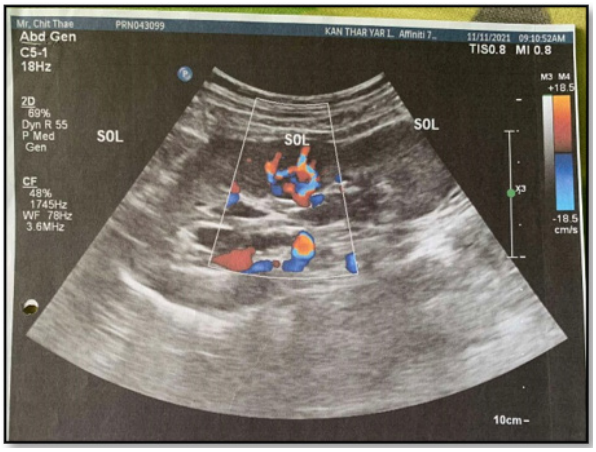

Figure 1: Ultrasound of graft kidney showing space occupying lesion.

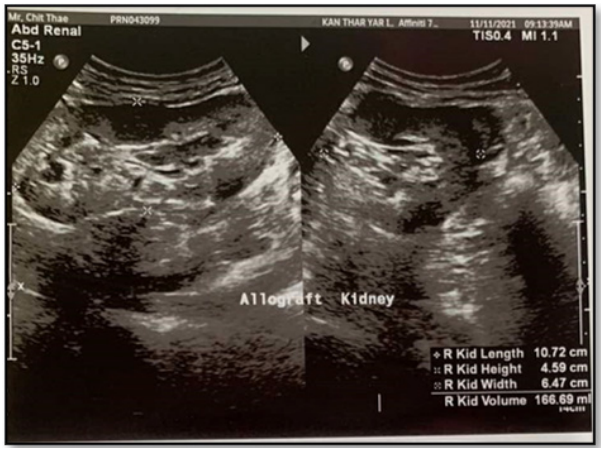

Figure 2: Ultrasound of graft kidney showing space occupying lesion.

In COVID-19 era, he did not attend follow up clinic. In November 2021, renal allograft function became impair; serum creatinine rose to 1.7mg/dl. In ultrasonogram, a well-defined smooth marginated ovoid hypoechoic lesion measuring about 2cm×1.6cm×2.1cm in dimension at middle cortex of allograft kidney was found. It was 4.7cm away from the upper pole and 4.9cm away from lower pole. No localized bulging seen at the site of lesion; it was not exophytic; increased color signal was noted. Figure 1 and 2 shows ultrasound of graft kidney with space occupying lesion. Computedtomographyrevealed enchancing rounded nodule 2×2cm was noted at lateral cortex of mid pole of transplant kidney; and there was no evidence of renal pelvic and other organ invasion. They are demonstrated in (Figure 3-5). They were suggestive of Renal Cell Carcinoma (RCC).

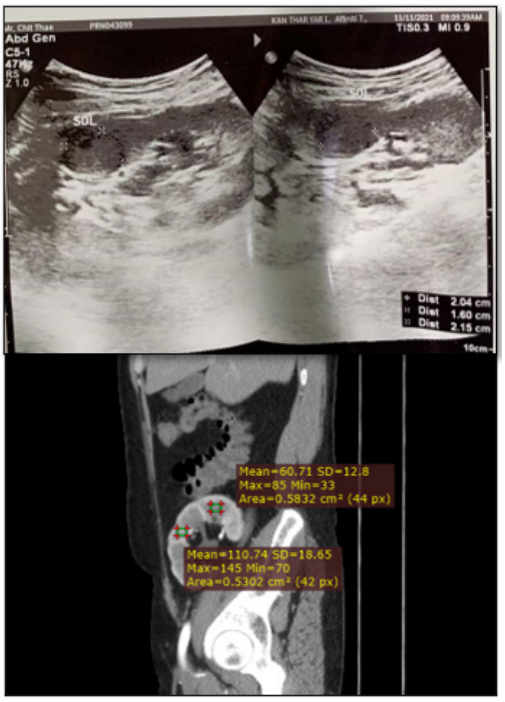

Figure 3: NECT sagittal view of abdomen showing graft kidney with space occupying lesion.

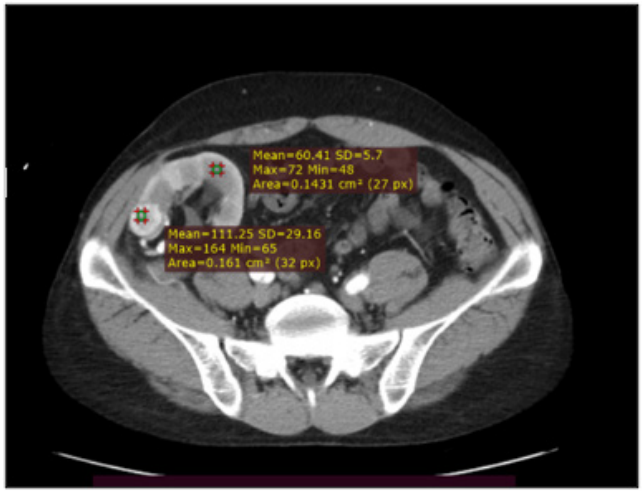

Figure 4: NECT axial view of abdomen showing graft kidney with space occupying lesion.

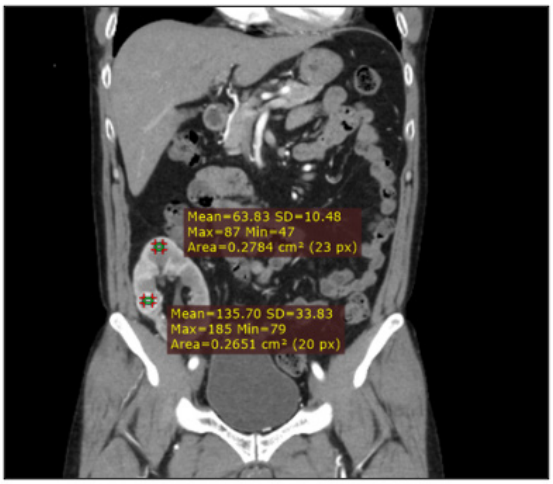

Figure 5: NECT coronal view of abdomen showing graft kidney with space occupying lesion.

Enucleation of suspected RCC area was done on 24 November 2021. Figure 6 reveals gross external appearance of enucleated mass. Histopathological examination was compatible with clear cell type of renal cell carcinoma; WHO/ISUPGrade I; and pT1-TNM classification. Microscopic findings are illustrated in (Figure 7-10). Maintenance immunosuppressant regimen was changed; cyclosporine was replaced with Everolimus.

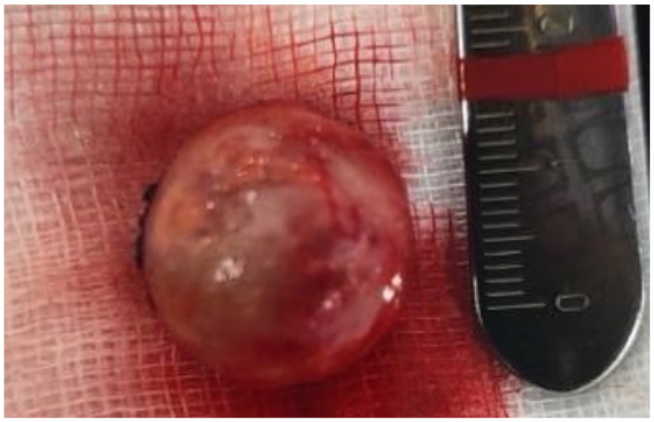

Figure 6: Macroscopic appearance of renal mass after removal.

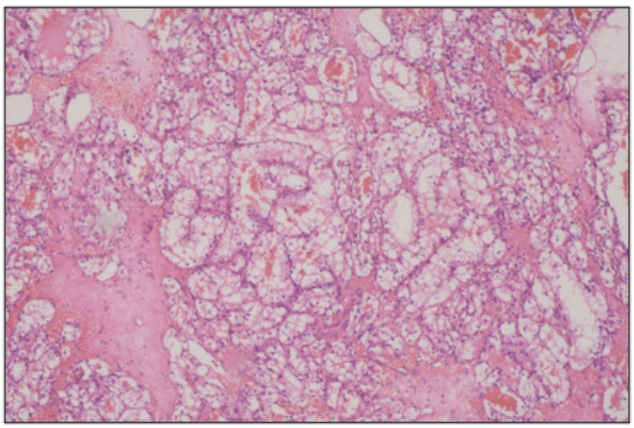

Figure 7: H&E stained of renal biopsy showing cluster of clear cells (Low resolution).

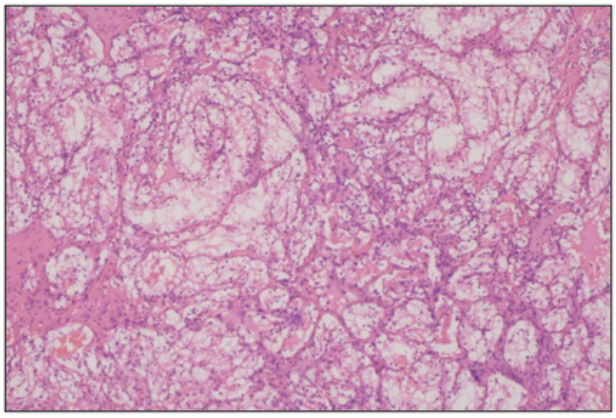

Figure 8: H&E stained of renal biopsy showing cluster of clear cells (Low resolution).

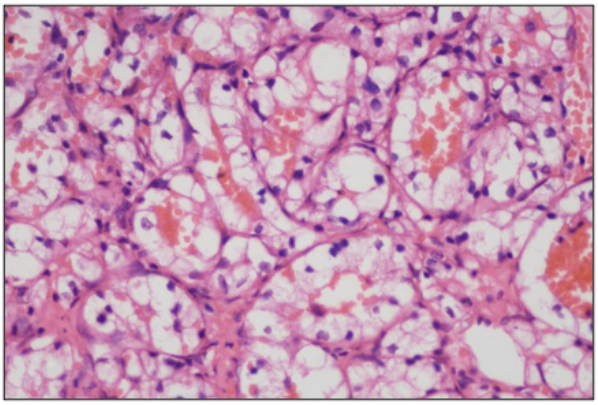

Figure 9: H&E stained of renal biopsy showing cluster of clear cells (High resolution).

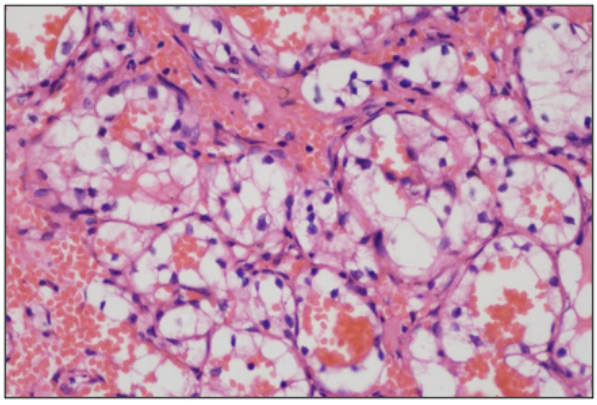

Figure 10: H&E stained of renal biopsy showing cluster of clear cells (High resolution).

After surgery, he was well; serum creatinine was 1.5mg/dl to 1.7mg/dl. For not normalization of serum creatinine level proteinuria, allograft renal biopsy was performed on 28 January 2022. And the graft histology was suggestive of Focal Segmental Glomerulosclerosis (FSGS) and IFTA score was approximately 60%. Graft histology features are shown in H&E (Figure 11), PAS stain (Figure 12) and silver stain (Figure13). Then, serum creatinine continued to rise gradually. He developed sepsis secondary to severe bronchopneumonia in March, 2023. Therefore, his creatinine became higher and ending up with End Stage Renal Disease again. And, he underwent maintenance hemodialysis. Second renal transplantation with living donor was done in November 2024. He was given ATG induction; and maintained with steroid, tacrolimus and mycophenolate. He had stable allograft function; serum creatinine was 0.9mg/dl.

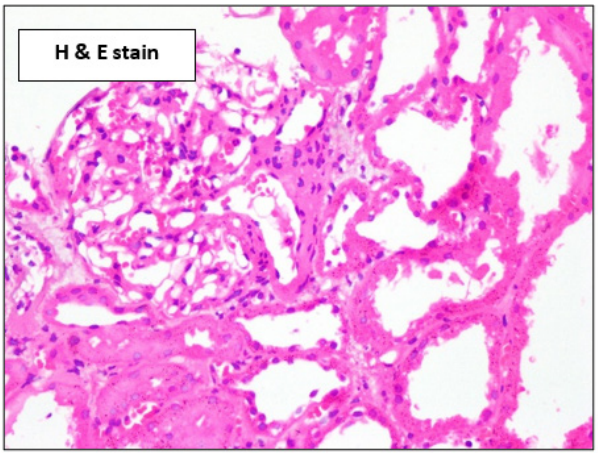

Figure 11: H&E stain of allograft biopsy showing a glomerulus with surrounding proximal tubules.

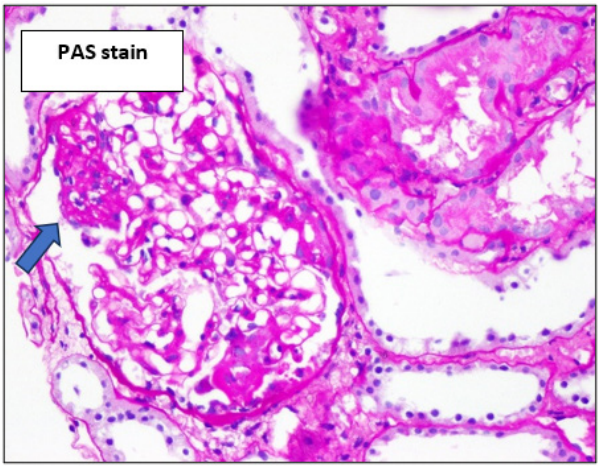

Figure 12a: PAS stain of allograft biopsy showing a glomerulus with segmental sclerosis and capsular adhesion (blue arrow indicates area of segmental sclerosis).

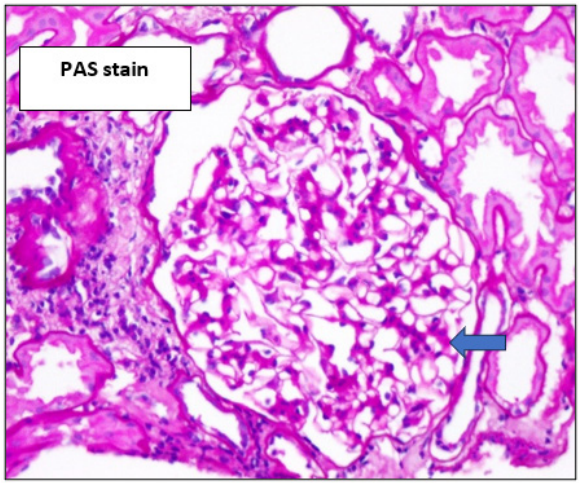

Figure 12b: PAS stain of allograft biopsy showing a glomerulus with segmental mild mesangial hypercellularity (blue arrow indicates area of mesangial hypercellularity).

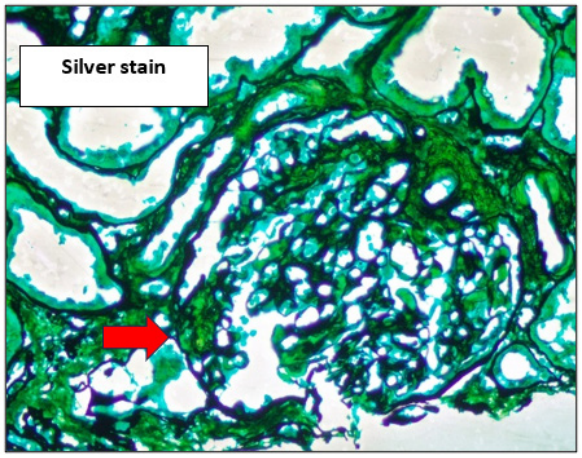

Figure 13: Silver stain of allograft biopsy showing a glomerulus with segmental sclerosis and capsular adhesion (red arrow indicates area of segmental sclerosis).

Discussion

Kidney transplantation is the optimal treatment modality for patients with End-Stage Renal Disease (ESRD). The long-term mortality of kidney transplant recipients is 50-80% lower than that of patients on the waiting list for transplant. On the other hand, the risk of cancer was higher in kidney transplant recipients [6]; the most common cancer was skin cancer, specifically Kaposi's sarcoma followed by hematological cancers.

In Myanmar Living Donor Kidney Transplant (LDKT) has been done since 1995; and Deceased Donor Kidney Transplant (DDKT) program has been trying in Myanmar. Nearly 500 renal transplant pairs have been successfully performed in military transplant centers which are situated in various States and Divisions; Yangon (Mingaladon), Northern Shan State (Pyin Oo Lwin), Central Myanmar (Nay Pyi Taw) and Southern Shan State (Aung Ban). Renal Transplant Ethical Committee allows both first degree and second-degree relatives as a donor for LDKT. Those who do not have close relatives may receive kidney from unrelated one. Renal Transplant Academic Committee has been screening malignancy to both donor and recipient with tumor markers and imaging. After transplant, the majority of renal transplant recipients have been attending follow up clinics at near-by transplant centers. This case was the first case of renal cell carcinoma (RCC) in graft kidney among them; five hundred living kidney transplant recipients done in military transplant centers in Myanmar. This is the main reason for case reporting.

Park et al reported that the risk of developing malignancies in kidney recipients was double compared to that of the healthy population. The incidence of Renal Cell Carcinoma (RCC) in kidney transplant recipients was found to be 10-30 times higher than that of non-transplanted patients [1]. Generally, the incidence of Renal Cell Carcinoma (RCC) in transplanted kidneys was reported as 0.2%. Therefore, this case was exceedingly rare. In kidney transplant recipients, RCC may develop either in their native kidneys or allografts. *Moris et al* reported that the incidence of RCC was higher in native kidneys than in allografts, 90% and 10% respectively [7]. This patient had RCC in graft kidney; therefore, it made a rare entity.

Risk factors for RCC in renal transplant were reported as follows: older age of the donors, smoking, obesity, hypertension and longer duration of transplant (more than 10 years) [2]. According to *Sebastian et al*, the incidence of allograft RCC was relatively higher in patients who received a kidney from a deceased donor than living donor transplant recipient [8]. Contrary to their findings, this patient received living kidney from his younger sister who was 31 years old; he did not smoke; he was not obese at the time of transplant. *Agraharkar et al* found that younger age at the time of transplant (less than 40 years) was related with risk of RCC [2]. The age of the patient at the time of transplant was twenty-four; and, RCC of graft kidney was diagnosed 10 years after transplant. Therefore, risk factors found in this case were comparable with the findings of [2].

The reasons for the increased risk of RCC in kidney transplant recipients were poorly understood. Several postulations were made; they were the impact of immunosuppression; changing tissue specificity in cancer driver genes in transplant patients; unknown oncogenic potential of donor renal tissue [9]. Therefore, *Dahle et al* highlighted the need for research on allograft RCC among kidney transplant recipients including genetic study [5]. In Myanmar military transplant centers, combination of prednisolone, azathioprine and cyclosporin was used as immunosuppressive regimen from 1995 to 2000; later, mycophenolate mofetil and tacrolimus were introduced gradually. This patient was prescribed prednisolone, mycophenolate mofetil and cyclosporin. Possible association between cyclosporin and malignancy was suggested in several studies. Following cyclosporin therapy, high risk of malignancy was reported in transplant recipients [10-13] as well as in patients with psoriasis [14]. The types of malignancy reported in them were skin cancer, lympho-proliferative disorder and solid organ tumor. In this

patient, taking cyclosporin therapy for 10 years might lead to RCC in graft kidney.

As of histological cell type of RCC in renal transplant recipients, the majority were clear cell carcinoma [15]. And, papillary RCC was rare form [16]. *Trushkin et al* found that transplanted kidney cancer originated from the donor tissue; and, the clear cell variant of transplanted kidney cancer was found to be genetically determined [4]. The majority of kidney transplant recipients with allograft RCC (75.4%) were found to be asymptomatic. The diagnosis of RCC in renal transplant recipients was incidental findings [3]. In this patient, the mass in allograft kidney was detected in follow-up after COVID era. And, the size was small (2cm). Therefore, regular screening was important [17-21].

Conclusion

Kidney transplant recipients typically have only one functioning kidney. And they have increased risk of malignancy compared to general population. Malignancy is third leading cause of death in kidney transplant recipients. Risk of RCC in renal transplant recipients is higher than general population in kidney transplant recipients. Post-transplant screening for RCC both in native kidneys and allograft kidney with annual ultrasonogram is essential to get early diagnosis of RCC. It is important for clinicians to heightened disease awareness.

Ethical Consideration

Informed consent was taken from patient.

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Conflict of Interest

None.

Funding

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