Presumed Monozygotic Twin Kidney Transplantation with a Thin Basement Membrane Nephropathy Donor: A Case Report

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ABSTRACT

Identical or Monozygotic twin kidney transplant usually possess an excellent immunological match and provide the opportunity to minimize or even avoid immunosuppression toxicity. However, there are concerns regarding disease recurrence among end stage kidney disease (ESKD) patients with an unknown etiology. Together with the risk of inherent, familial disease affecting donors and recipients alike, more invasive tests such as a pretransplant biopsy are being considered to ascertain renal prognosis.

A 30-year-old female, known case of CKD Stage 5D from an unknown etiology, with secondary hyperparathyroidism and heart failure, presented at our OPD for kidney transplantation. Her donor is her identical twin who is asymptomatic and denies comorbidities. The recipient discloses a previous history of blood transfusion.

Immunological workup revealed the following: matched blood type, zero HLA mismatch, negative T-cell tissue crossmatch but with a positive Class I HLA antigen screen. Antibody specificity revealed the presence of donor specific antibodies (DSA). After workup completion, the patient underwent a right kidney transplant with a preimplantation wedge biopsy on the donor kidney. Immediate graft function was noted post operatively. The wedge biopsy revealed a thinned glomerular basement membrane, consistent with Thin Basement Membrane Nephropathy (TBMN).

The patient was started on immunosuppression and prophylaxis during the duration of the post operative period without any complications. Five months post-transplant, both the recipient and donor maintain an adequate renal function without any signs of allograft rejection.

In this case report, we have demonstrated that TBMN may serve as a viable donor for a presumed monozygous twin kidney transplantation. When a live donor with TBMN is being considered, a thorough work-up and identification of high-risk features are essential to exclude other progressive renal diseases during the pretransplant evaluation.

Keywords: Kidney transplantation, thin basement membrane nephropathy, glomerulonephritis, case report

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INTRODUCTION

Identical or monozygotic twin kidney transplant presents a unique clinical scenario. It is considered the ideal transplant, possessing an excellent immunological match and the opportunity to minimize and even avoid immunosuppression toxicity. However, there are concerns regarding

primary disease recurrence among end stage kidney disease (ESKD) patients with an unknown etiology.[1,2] Together with the risk of inherent, familial disease affecting donors and recipients alike, considerations for more invasive tests such as a pretransplant biopsy are being done to ascertain renal prognosis.[3]

Here we present a presumed monozygotic twin kidney transplant that underwent an intraoperative preimplantation biopsy revealing a subclinical thin basement membrane nephropathy (TBMN) of the donor kidney. In this case report, we discuss the clinical issues we encountered and review the current literature surrounding the viability of TBMN donors.

CASE PRESENTATION

A 30-year-old Filipino female, known case of chronic kidney disease stage 5D secondary to chronic glomerulonephritis (no previous biopsy done) and maintained on hemodialysis, presented at our outpatient clinics for kidney transplantation. She is also a diagnosed case of secondary hyperparathyroidism on cinacalcet (90 mg/day) and heart failure with reduced ejection fraction (46%) secondary to cardiorenal syndrome type IV maintained on carvedilol (50 mg/day) and sacubitril/valsartan (100 mg/day). A review of her family history was unremarkable for hereditary kidney disease. The patient had a history of blood transfusion with two units of packed red blood cells (pRBC) the year prior but denies previous history of kidney transplantation or pregnancies. Her donor is her identical twin, a 30-year-old female who is asymptomatic and denies comorbidities or intake of any medication.

Immunological workup revealed the following: matched blood type (O+), 0/6 human leukocyte antigen (HLA) mismatch, negative T-cell tissue crossmatch but with a positive Class I HLA antigen screen with calculated panel reactive antibody (cPRA) score of 5%. A Class I single antigen bead (SAB) assay noted the following donor specific antibodies (DSA) present in the recipient (Table 1). Donor workup showed a 24-hour urine protein of 176 grams, negative urine dipstick blood, urine red blood cell (RBC) count 1-2 per high power field (HPF), and a urine white blood cell (WBC) count 0-2 per high power field (HPF). Renal CT Angiography noted unremarkable left and right kidneys in terms of location, length, thickness and orientation, without stones, mass or vascular anomalies. Both kidneys are also supplied by a single renal artery and vein.

After completion of the immunological and ancillary workup, the patient was scheduled to undergo kidney transplant. However, given the undocumented etiology of the recipient's renal failure and identical twin relationship of the donor and recipient, the medical team suggested to perform an intraoperative kidney biopsy prior to reperfusion. With consent from the recipient and an unremarkable donor kidney workup, the transplant team decided to proceed with a right kidney transplant with an intraoperative renal wedge biopsy. Immediate graft function was noted with a urine output of 340 ml during the first post operative hour. Cold ischemia time was recorded at fifteen minutes and fifty-two seconds with a warm ischemia time of thirty-six minutes and eleven seconds.

Table 1. Immunological Matching and Workup

	Recepient	Donor
Blood typing	O+	O+
HLA Typing		
A Locus	24(9), 23(9)	24(9), 23(9)
B Locus	51(5), 61(40)	51(5), 61(40)
DR Locus	12(5), 15(2), 51, 52	12(5), 15(2), 51, 52
DQ Locus	5(1)	5(1)
HLA Antibody Screening		
Class I	Positive	-
Class II	Negative	-
MICA	Negative	-
HLA Antibody Specificity Testing and corresponding Mean fluorescence intensity (MFI)	cPRA = 5% Cw4 – 2972 A66(28) – 578 A43 – 1106 A26(10) – 553 Cw2 – 959 A32(19) – 374 Cw1 – 815 A33(19) – 302 A34(10) – 737 A25(10) – 260	
T-cell Tissue Crossmatching		
Amos	Negative	Negative
Anti-Kappa	Negative	Negative

Abbreviations: HLA, Human leukocyte antigen; MICA, major histocompatibility complex class I chain-related gene A; MFI, Mean fluorescence intensity; cPRA, calculated panel reactive antibody

The patient was started on rabbit anti-thymocyte globulin (rATG, 25 mg/day for three days) with methylprednisolone (500 mg/day for three days), tacrolimus (2 mg/day) and mycophenolic acid (720 mg/day). Methylprednisolone was eventually shifted to prednisone (40 mg/day, 1 mg/kg/day) tapered by 5 mg/day until discharge (Figure 1). The patient was also given isoniazid (300 mg/day), valacyclovir (800 mg four times a day), nystatin (500,000 units thrice a day) and trimethoprim-sulfamethoxazole (800 mg / 160 mg every other day) as prophylaxis.

The renal biopsy yielded 48 glomeruli for examination and demonstrated the following: on light microscopy, the glomeruli were generally unremarkable with no endocapillary or extracapillary proliferation (Figures 2A and 2B). Immunofluorescence revealed diffuse, segmental, granular, mesangial staining for IgG, IgA, IgM, trace fibrinogen and C3, focal granular vascular staining and a negative C1q staining (Figure 3). Electron microscopy showed mean glomerular basement membrane thickness at 231 nm with intact podocyte foot processes (Figures 4A and 4B) and occasional

paramesangial and mesangial electron-dense deposits without substructure (Figure 5). Overall, the findings were found to be consistent with a thin basement membrane disease.

Five months post-transplant, the recipient was able to maintain good renal function and is now on prednisone (2.5 mg/day), mycophenolic acid (720 mg/day), and tacrolimus (4 mg/day, targeting a C_0 tacrolimus trough level between 3-7 ng/mL). Latest laboratory examinations show a serum creatinine 0.41 mg/dL, hemoglobin 130 g/dL, negative urine dipstick protein and blood, and a urine RBC 0-2/HPF, WBC 0-1/HPF. The donor is currently asymptomatic with a serum creatinine of 0.68 mg/dL and unremarkable urinalysis findings. Moving forward, we plan on confirming monozygosity with DNA analysis and gradually withdraw immunosuppression as tolerated. We also intend to do a thorough work-up on the family of the patients and perform genetic testing to rule out familial causes of ESKD of unknown origin.

DISCUSSION

Clinical and histologic status of donors are known to influence graft outcomes after kidney transplantation. There are cases wherein an unsuspected renal pathology

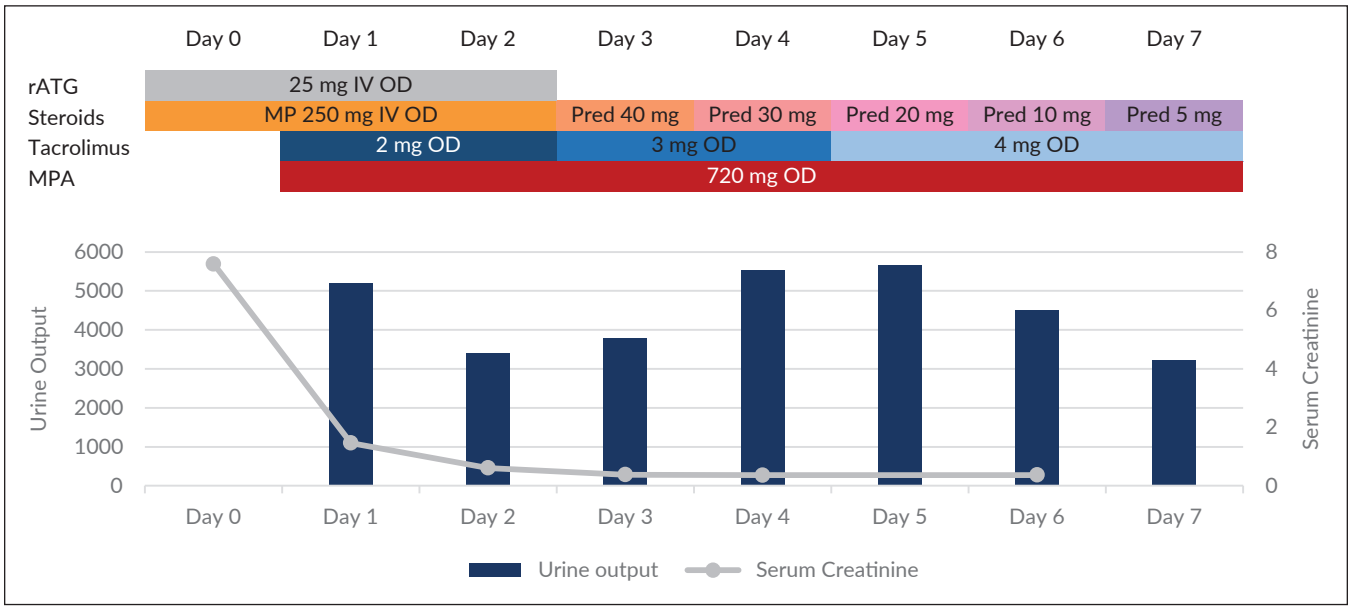

Figure 1. Serum creatinine and urine output trends after kidney transplant with corresponding immunosuppressive regimen used.

rATG, rabbit anti-thymocyte globulin; OD, once a day; MP, Methylprednisolone; Pred, Prednisone; MPA, mycophenolic acid; IV, intravenous

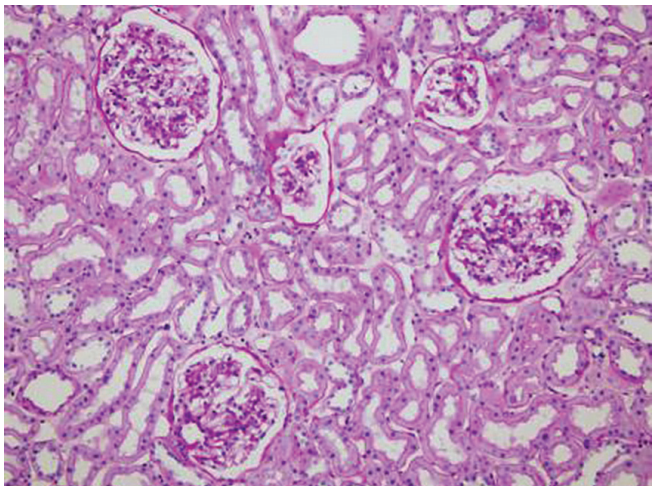

Figure 2A. ***Light microscopy.*** Generally unremakable glomeruli and interstitium (Periodic Acid Schiff stain, x20).

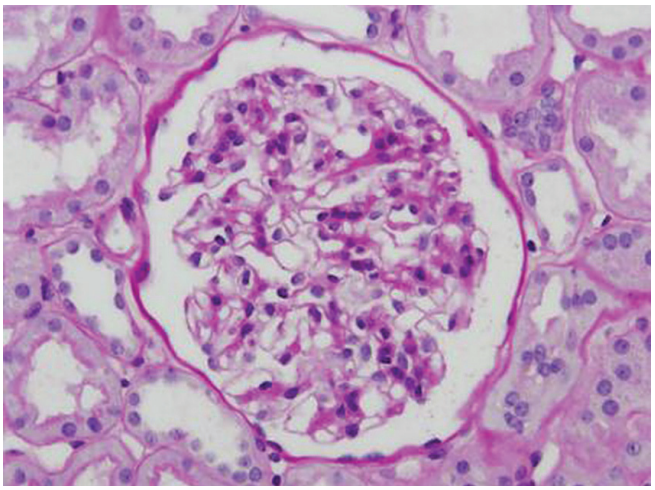

Figure 2B. ***Light microscopy.*** Representative glomeruli demonstrating unremarkable view (Periodic Acid Schiff stain, x60).

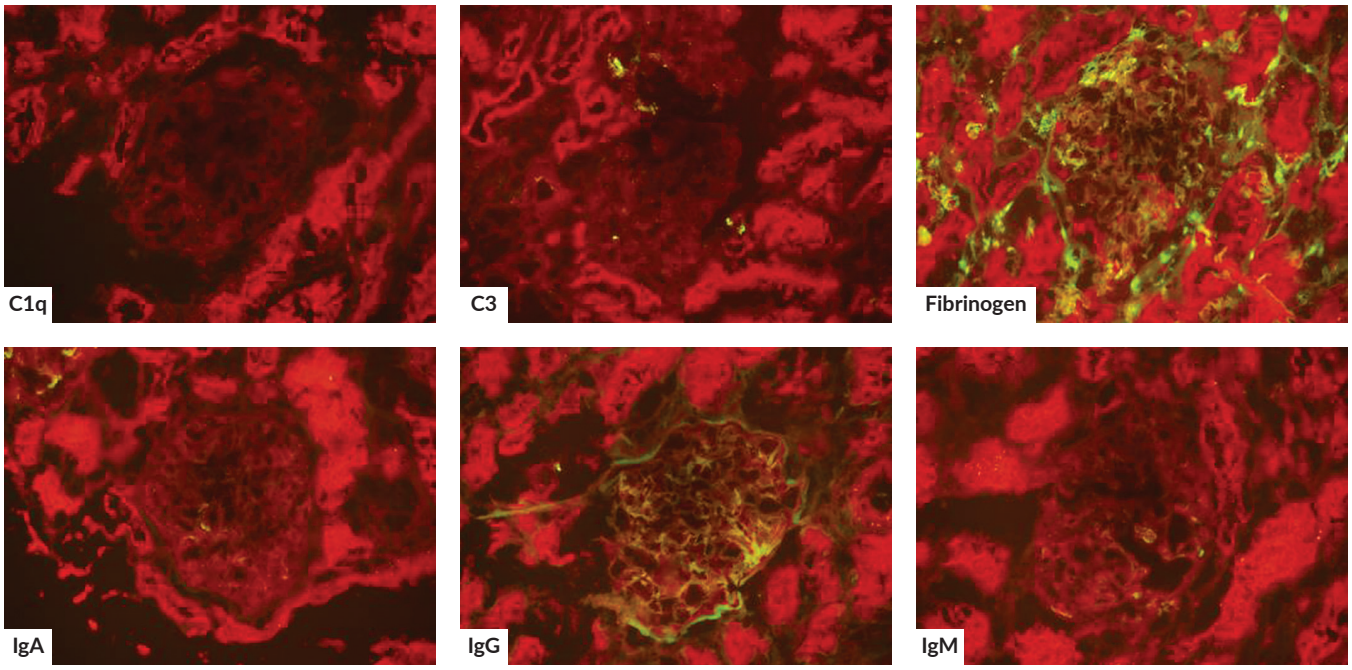

Figure 3. Immunofluorescence staining showing negative C1q staining, diffuse segmental granular mesangial C3 staining (trace), and diffuse segmental granular mesangial staining for fibrinogen, IgA, IgG, IgM, (trace).

was reported in donor kidneys, despite thorough pre-transplant evaluation.[4] Subclinical kidney damage poses a risk for progressive renal dysfunction and possible ESKD in donors, and allograft rejection among recipients.[5] Certain donor characteristics such as older age and lower glomerular filtration rates, may predict the risk of graft failure, however, these sometimes fail to reflect underlying structural features in the kidney that may aid in predicting graft longevity.[6]

Although not considered routine, preimplantation renal biopsies can evaluate the impact of histologic abnormalities on the immediate and possible long-term renal function, at the moment of donation.[7] It may identify microstructural features, subclinical lesions, and pathologic changes that may impact prognosis and can be transmitted from the donor to recipient via the grafted kidney, act as a baseline biopsy for comparing morphology with subsequent graft biopsies, and offer useful additional information when the donor kidney is considered marginal.[8-11] We decided to perform a preimplantation kidney biopsy to ascertain possible renal disease from the allograft since our recipient has a suspected glomerulonephritis as an underlying etiology of ESKD. As our recipient and donor are closely related, both are at an increased risk for adverse outcomes should the biopsy present with significant renal pathologies and high-risk features. Renoprotective interventions, intensive immunosuppression, and closer monitoring may also be performed earlier, should the need arise. Thus, it is prudent to exclude any subclinical disease that may be present in the donor kidney, despite having an unremarkable pretransplant evaluation.[11,12]

Post procedure, the biopsy of our renal allograft revealed a thin basement membrane nephropathy (TBMN). TBMN is a common cause of persistent glomerular bleeding among adults and is often found incidentally during renal biopsy.[13] Clinically, patients usually present with hematuria, minimal proteinuria, and normal renal function.[14] On electron microscopy, the glomerular basement membrane thinning measures <250 nm and affects more than 50% of glomeruli and at least 50% of individual capillary loops.[13] While TBMN is generally considered a benign, nonprogressive disorder, donations from individuals with the disease remain controversial due to limited studies addressing the long-term prognosis of donors and recipients.[14] In a retrospective study of kidney transplant donors demonstrating TBMN on biopsy, ten out of eleven renal grafts showed normal glomerular basement membrane without any signs of rejection throughout the entire follow-up period (56.8 ± 32.0 months). All donors were able to maintain an adequate renal function without kidney-related complications.[14] Koushik et al. reported short-term follow-up results from two transplant recipients from donors with TBMN. Neither the recipients nor the donors experienced significant renal dysfunction at 15 and 16 months.[15] In general, patients with TBMN and atypical features such as proteinuria, hypertension, or overt renal insufficiency, should not be donors. A family history of hematuria and presence of extrarenal manifestations may also help identify and differentiate progressive renal diseases.[13] In our case, the absence of donor features suggestive of a renal disease on clinical evaluation and laboratory workup, together with an excellent immunological match, may point

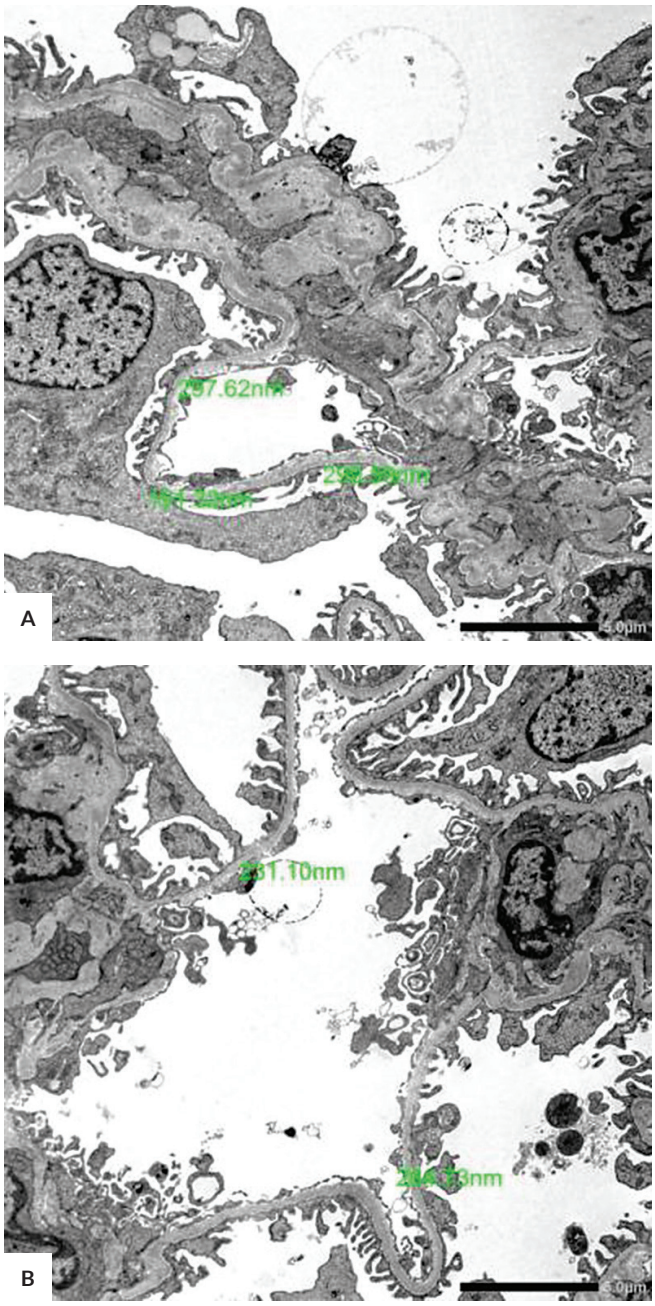

Figure 4. Electron microscopy views demonstrating areas of glomerular basement membrane thinning.

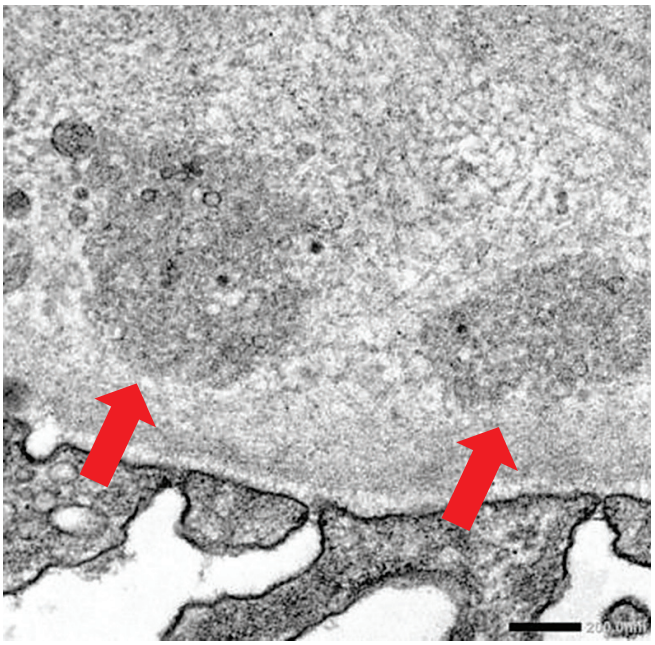

Figure 5. Paramesangial and mesangial electron-dense deposits without notable substructure *(red arrows)*.

to a lower risk of renal disease progression and eventual renal failure despite the histologic findings of TBMN. However, given the short-term follow-up and the limitations on the studies on TBMN donors, close monitoring is still needed. As of the latest follow-up, both donor and recipient remain asymptomatic with preserved renal function.

Postoperatively, we decided on immunosuppression despite the current evidence of low-risk allograft rejection and excellent graft survival among monozygotic twin transplants, even among immunosuppression free patients.[1,2,16-18] This is due to the presence of Class I DSAs in our recipient, likely from her previous history of sensitization (blood transfusion). Together with the pair's undetermined zygosity, these factors pose a risk of rejection after transplant.[1,16,19] There is no consensus on the use of immunosuppression following twin transplantation, however performing DNA zygosity tests, such as STR analysis, has been suggested to assess the need to administer, continue or stop maintenance immunosuppressive therapy.[1] We eventually plan to perform confirmatory DNA testing in order to wean the recipient off immunosuppression.

CONCLUSION

In this case report, we have demonstrated that TBMN may serve as a viable donor for a presumed monozygous twin kidney transplantation. When a live donor with TBMN is being considered, a thorough work-up and identification of high-risk features are essential to exclude other progressive renal diseases during the pretransplant evaluation.

Ethical Considerations

Informed consent was obtained from the donor and recipient for publication of this report and all identifying information has been removed to protect the patient's privacy.

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Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

The authors declare that they have no conflicts of interest with respect to the research, authorship, and/or publication of this case report.

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REFERENCES

1. Jorgensen DR, Wu CM, Hariharan S. Epidemiology of end-stage renal failure among twins and diagnosis, management, and current outcomes of kidney transplantation between identical twins. Am J Transplant. 2020 Mar;20(3):761-8. doi: 10.1111/ajt.15638.
2. Kessaris N, Mukherjee D, Chandak P, Mamode N. Renal transplantation in identical twins in United States and United Kingdom. Transplantation. 2008 Dec;86(11):1572-7. doi: 10.1097/TP.0b013e31818bd83d.
3. Naesens M. Zero-time renal transplant biopsies: a comprehensive review. Transplantation. 2016 Jul;100(7):1425-39. doi: 10.1097/TP.0000000000001018.
4. Lee AL, Kim YS, Lim BJ, Jeong HJ, Joo DJ, Kim MS, et al. The impact of time-zero biopsy on early graft outcomes after living donor kidney transplantation. Transplant Proc. 2013 Oct;45(8):2937-40. doi: 10.1016/j.transproceed.2013.08.081.
5. van der Weijden J, de Borst MH. Tissue is the issue: kidney biopsy findings and long-term outcomes in living kidney donors. Mayo Clin Proc. 2021 Jan;96(1):10-12. doi: 10.1016/j.mayocp.2020.11.011.
6. Issa N, Lopez CL, Denic A, Taler SJ, Larson JJ, Kremers WK, et al. Kidney structural features from living donors predict graft failure in the recipient. J Am Soc Nephrol. 2020 Feb;31(2):415-23. doi: 10.1681/ASN.2019090964.
7. Mancilla E, Avila-Casado C, Uribe-Uribe N, Morales-Buenrostro LE, Rodríguez F, Vilatoba M, et al. Time-zero renal biopsy in living kidney transplantation: a valuable opportunity to correlate predonation clinical data with histological abnormalities. Transplantation. 2008 Dec;86(12):1684-8. doi: 10.1097/TP.0b013e3181906150.
8. Merzkani MA, Denic A, Narasimhan R, Lopez CL, Larson JJ, Kremers WK, et al. Kidney microstructural features at the time of donation predict long-term risk of chronic kidney disease in living kidney donors. Mayo Clin Proc. 2021 Jan;96(1):40-51. doi: 10.1016/j.mayocp.2020.08.041.
9. Rathore RS, Mehta N, Mehta SB, Babu M, Bansal D, Pillai BS, et al. Can zero-hour cortical biopsy predict early graft outcomes after living donor renal transplantation? Can Urol Assoc J. 2017 Nov;11(11):E437-E440. doi: 10.5489/cuaj.4506.
10. Randhawa P. Role of donor kidney biopsies in renal transplantation. Transplantation. 2001 May;71(10):1361-5. doi: 10.1097/00007890-200105270-00001.
11. Wang CJ, Wetmore JB, Crary GS, Kasiske BL. The donor kidney biopsy and its implications in predicting graft outcomes: a systematic review. Am J Transplant. 2015 Jul;15(7):1903-14. doi: 10.1111/ajt.13213.
12. Fahmy LM, Massie AB, Muzaale AD, Bagnasco SM, Orandi BJ, Alejo JL, et al. Long-term renal function in living kidney donors who had histological abnormalities at donation. Transplantation. 2016 Jun;100(6):1294-8. doi: 10.1097/TP.0000000000001236.
13. Ierino FL, Kanellis J. Thin basement membrane nephropathy and renal transplantation. Semin Nephrol. 2005 May;25(3):184-7. doi: 10.1016/j.semnephrol.2005.01.012.
14. Choi C, Ahn S, Min SK, Ha J, Ahn C, Kim Y, et al. Midterm outcome of kidney transplantation from donors with thin basement membrane nephropathy. Transplantation. 2018 Apr;102(4):e180-e184. doi: 10.1097/TP.0000000000002089.
15. Koushik R, Garvey C, Manivel JC, Matas AJ, Kasiske BL. Persistent, asymptomatic, microscopic hematuria in prospective kidney donors. Transplantation. 2005 Nov;80(10):1425-9. doi: 10.1097/01.tp.0000181098.56617.b2.
16. Yakubu I, Haririan A, Bartlett S, Sparkes T. Successful renal transplantation between identical twins with very brief immunosuppression. Case Rep Transplant. 2018 Jun;2018:9842893. doi: 10.1155/2018/9842893.
17. Sánchez-Escuredo A, Barajas A, Revuelta I, Blasco M, Cofan F, Esforzado N, et al. Kidney transplant from a living monozygotic twin donor with no maintenance immunosuppression. Nefrologia. 2015;35(4):358-62. doi: 10.1016/j.nefro.2015.06.006.
18. Krishnan N, Buchanan PM, Dzebisashvili N, Xiao H, Schnitzler MA, Brennan DC. Monozygotic transplantation: concerns and opportunities. Am J Transplant. 2008 Nov;8(11):2343-51. doi: 10.1111/j.1600-6143.2008.02378.x.
19. Alelign T, Ahmed MM, Bobosha K, Tadesse Y, Howe R, Petros B. Kidney transplantation: the challenge of human leukocyte antigen and its therapeutic strategies. J Immunol Res. 2018 Mar;2018:5986740. doi: 10.1155/2018/5986740.