Prolonged renal allograft survival without immunosuppressive therapy

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To the Editor,

A 47-year-old White man with a history of renal transplantation was seen in the Nephrology clinic for worsening renal function and proteinuria. He was born with a single kidney with anatomic abnormalities leading to frequent urinary tract infections and end-stage renal disease by age 16. At that time, he received a kidney transplant from a deceased donor, but the allograft failed in 6 years, apparently due to cyclosporine toxicity. At age 22, he received a living-related kidney transplant from his sister. There were 3 out of 6 HLA loci mismatches, one each for A, B and DR between the patient and his sister and he received induction therapy with anti-thymocyte globulin. 4 years later, he had allograft nephrectomy of the first transplant due to pain and shortly thereafter, he stopped taking all his immunosuppressive medications because he lost his insurance and could not afford them. He had no kidney-related issues or hospitalizations for the next 20 years, and 1 year prior to current presentation, he saw a general physician for pedal edema. His serum creatinine was ~1.5 mg/dL at that time with an elevated blood pressure. He was treated with a loop diuretic and lisinopril. Renal function progressively worsened during the course of the year, and his serum creatinine was 2.9 mg/dL with urine protein–creatinine ratio of 6 g/g (Ref: <150 mg/g) at presentation. Serologic testing for human immunodeficiency virus, viral hepatitis and syphilis was negative. Biopsy of the renal allograft revealed transplant glomerulopathy, moderate interstitial fibrosis and no acute rejection (Fig. 1). Immunohistochemical staining for C4d was positive along glomerular capillary loops (3 +) but the

staining of peritubular capillaries was negative. There was no tubulitis or peritubular capillaritis. Further serological testing revealed post-transplant donor-specific antibodies to his sister: A29 (moderately strong), DR 53 (strong) and DQ3/4 (strong). He also had a Calculated Panel Reactive Antibodies (CPRA) of 97%. We maximized the angiotensin-converting enzyme inhibitor therapy; also plan to start the immunosuppressive therapy in anticipation of a retransplant.

Transplant glomerulopathy is an important cause of worsening creatinine, proteinuria, hypertension, and shortened allograft survival. Histologically, it is characterized by reduplication or multilamination of glomerular basement membrane in the absence of immune-complex deposits, identifiable on light microscopy using periodic acid Schiff or silver staining [1]. Chronic, repeated endothelial cell injury is thought to result in this lesion, which is typically associated with chronic antibody-mediated rejection. Unfortunately, there is no specific treatment proven to work for transplant glomerulopathy and supportive measures given to any patient with chronic kidney disease remain the mainstay of management [2]. What is unusual about our case is that the patient had functioning graft for more than the mean lifespan of a living donor kidney (typically around 12–20 years) without immunosuppressive therapy. In general, stable graft function without clinical features of chronic rejection in the absence of any immunosuppressive drugs for more than 1 year is defined as spontaneous operational tolerance. While the time frame is debatable and some experts exclude patients with transplant glomerulopathy from this definition, it is not clear why some patients are more tolerant to allograft than others. Living-related donor and young donor age are thought to be favorable factors, both of which, our patient had [3]. Moreover, he did not have traditional risk factors for chronic kidney disease such as long-standing hypertension and diabetes mellitus. Future studies with larger number of tolerant individuals are needed to better understand the immunologic mechanisms behind this phenomenon.

Author contributions

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Fig. 1 Renal biopsy demonstrating **a** relatively normocellular glomerulus with increase in mesangial matrix [H&E]; **b** thick glomerular capillary loops with extensive “double contour” appearance [PAS

stain]; **c** moderate tubular atrophy and interstitial fibrosis without findings suggestive of acute rejection [H&E]

The authors have made substantial contribution to the preparation of this manuscript.

Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

Human and animal rights (with IRB approval number) This article does not contain any studies with human participants or animals performed by any of the authors. IRB approval is not applicable for a letter/single case study.

Registration of clinical trials Not applicable.

Informed consent Informed consent was obtained for the publication of this case study.

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