IgA nephropathy in identical twins: an excellent donor and recipient outcome 11 years after transplantation

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Abstract
We present a case of IgA nephropathy (IgAN) in monozygotic twins with excellent donor and recipient outcome 11 years after transplantation. The recipient developed IgAN at 26 years and progressed to end-stage renal failure 10 years later. His identical twin who had hypertension, intermittent microscopic haematuria and positive IgA immunofluorescence on biopsy became his donor. Eleven years following transplant, in the absence of immunosuppression, the recipient has stable graft function [estimated glomerular filtration rate (eGFR) 47 mL/min/1.73 m², Modification of Diet in Renal Disease (MDRD)], controlled hypertension on two medications and minor microscopic haematuria. The donor has good renal function (eGFR 51 mL/min/1.73 m², MDRD), controlled hypertension on one medication and normal urine.

Keywords: background; IgA nephropathy; kidney; monozygotic twin; transplantation

Background
IgA nephropathy (IgAN) is one of the most common types of glomerulonephritis worldwide [1]. IgAN causes a broad range of disease phenotypes from non-progressive mild urinary abnormalities to rapidly progressive crescentic glomerulonephritis. IgAN may occur in renal allografts and is either de novo, recurrent or donor-transmitted [2]. We report a case of IgAN affecting a donor recipient pair of identical twins with excellent 11-year outcome.

Case report
A 26-year-old man presented in 1988 with hypertension (180/100 mmHg), normal urine microscopy, proteinuria (2.2 g/24 h) and preserved renal function (radionuclide glomerular filtration rate 84 mL/min/1.73 m²). A percutaneous renal biopsy showed IgAN. Immunofluorescence was strongly positive for mesangial IgA and large electron-dense deposits were seen in the paramegasonium and basement membrane subendothelialy. He received an angiotensin-converting enzyme inhibitor and diuretic.

The patient developed slowly progressive renal impairment over 10 years. A monozygotic twin wished to be considered for pre-emptive kidney donation. The twin had treated hypertension. His hypertension had been investigated 9 years earlier at which time he did not have microscopic haematuria.

The identical twin completed living donor assessment. He had intermittent microscopic haematuria (55 × 10⁶/L, red cells, no dysmorphic red cells), no proteinuria, controlled hypertension (140/80 mmHg on 10 mg of quinapril), normal echocardiogram and 24-h urine creatinine clearance 168 mL/min. A kidney biopsy showed occasional glomeruli with a slight increase in mesangial matrix but no glomerulosclerosis, interstitial fibrosis or vasculopathy. Immunofluorescence was positive for IgA. Monozygotic twin status was confirmed by testing with nine highly polymorphic short tandem repeat loci.

We discussed the risks and benefits of proceeding with transplantation with the donor and recipient. Two opinions were sought from international experts on IgAN. One supported proceeding—'it is difficult to present a convincing argument why they should not proceed, provided they understand the potential risks involved, both to the transplanted kidney and to the donor' (Sir Peter Morris, Surgeon, Oxford, personal communication). The second opinion recommended not proceeding based on personal experience from three unpublished cases with poor outcomes (Dr A.R. Clarkson, Nephrologist, Adelaide, personal communication). The first case was an identical twin transplant where the donor (previously asymptomatic) developed the disease in his single remaining kidney reaching end-stage renal failure, requiring transplantation within 2 years. The second case was a cadaveric graft containing IgA deposits (found on insertion biopsy) transplanted into an IgAN recipient with significant early recurrence. The third case was a patient with IgAN with a single functioning kidney that had a quicker than expected decline in renal function following diagnosis.

This information in addition to the medical findings was discussed with the donor, recipient and their families.
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were felt to understand the risks and uncertainties and therefore be in a position to make an informed decision. They decided to proceed. The operation and immediate recovery were uncomplicated. A graft biopsy at implantation and then 1 month later showed findings consistent with the donor pre-transplant assessment biopsy.

Eleven years later, both donor and recipient are well at the age of 50 years. The donor’s serum creatinine is currently 129 µmol/L [estimated glomerular filtration rate (eGFR) 51 mL/min/1.73 m², Modification of Diet in Renal Disease (MDRD)]. The donor’s blood pressure is controlled (140/85 mmHg) taking quinapril 10 mg daily. Urinalysis is normal. The recipient has a serum creatinine of 140 µmol/L (eGFR 47 mL/min/1.73 m², MDRD), blood pressure of 130/88 mmHg on two agents. Urinalysis shows 10–20 × 10³/L red cells and 2+ protein on dipstick.

Discussion

This case highlights identical twins with contrasting IgAN phenotype and kidney donation between them. We are not aware of a published case in which a kidney transplant recipient was simultaneously at risk for both recurrent and donor-transmitted IgAN in monozygotic twins with the donor known to have IgAN prior to donation.

Recurrent IgAN occurs in up to 35% of allografts with similar 10-year graft survival to de novo IgAN [3]. A genetically identical donor might increase the risk of recurrent disease. In a case series on IgAN in living-related donors, one recipient with crescentric IgAN received a healthy kidney from her identical twin. Eleven years later, graft biopsy showed mesangial IgA deposits, and the recipient had renal impairment with haematuria and proteinuria. Two years and 6 months after donation, the identical twin donor had traces of proteinuria [4].

IgAN may be transmitted to a recipient. A series of six cases of donor-transmitted IgAN identified on biopsies 1 h to Day 3 post-transplant had good outcomes. No graft was lost but two developed proteinuria and haematuria with one having a serum creatinine over 176 µmol/L [5]. A case series of eight recipients confirmed a favourable prognosis of donor-transmitted IgAN in the recipients without IgAN. Mesangial deposits disappeared in most cases and graft function was good in all cases [6].

IgAN can have an excellent prognosis but long-term prognosis for donors with IgAN is unclear. There are no prospective studies on living-related donors with a complete morphologic study at the time of donation, and therefore, the prognosis for these living donors with IgA glomerular deposits in their remaining kidney is not clear [4]. Koselj et al. [7] published a case series of three living-related kidney donors with silent IgAN, observed for 7 years. The first and second donor had a good outcome. By 1 year, the third donor had developed hypertension, proteinuria >1 g/24 h and intermittent haematuria. His kidney function deteriorated steadily with a creatinine of 880 µmol/L by 7 years. They suggest that IgAN superimposed on a reduced nephron status may be associated with a progressive course of disease [7].

Another study from the USA found persistent, asymptomatic, microscopic haematuria is uncommon in healthy prospective donors, but abnormalities were found on kidney biopsy in a high proportion of cases. Many may be unacceptable for donation but some may have mild lesions whose long-term risk in the absence of donation is likely to be low. In this situation, extensive discussion and counselling are felt to be appropriate [8].

This case is interesting in several ways. There was uncertainty around the risk to the donor and the decision to proceed. The donor had biopsy-proven IgAN diagnosed prior to donation. He had several good prognostic indicators (lack of proteinuria or glomerulosclerosis and preserved renal function). Given the presumed existence of susceptibility genes, which will be identical to the recipient and the likely hyperfiltration associated with a single kidney, then the donor could be expected to have an increased risk of end-stage renal disease from IgAN relative to others with good prognostic indicators. This information and the uncertainty were balanced against the donor’s right to autonomy in decision-making around donation. The recipient received a genetically identical kidney with biopsy-proven IgAN and is at risk of both donor-transmitted and recurrent IgAN (which would be indistinguishable). No immunosuppression is required in genetically identical twin recipients but the effect of withholding immunosuppression on IgAN in the graft was unknown. Eleven years after transplantation, the donor has stable renal function, well-controlled blood pressure and low risk for progressive renal impairment. It is likely the recipient has IgAN in the graft but whether this is donor-transmitted or recurrent disease is unclear. The recipient has benefited from kidney transplantation without long-term immunosuppression, and the donor has achieved his aim of donating to his brother without sequelae.

Conflict of interest statement

None declared.

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