Reminder of important clinical lesson

Kidney transplantation among identical twins: therapeutic dilemmas

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Summary

A case of the successful kidney transplantation among two homozygous twins is presented here. Prior to the familial kidney transplantation from the identical twins, the patient underwent peritoneal and haemodialyses as well as cadaveric kidney transplant from an unrelated donor. In this patient, vascular accessibility was poor and the second familial transplantation was performed urgently. Transplanted kidney function proved excellent; however, the issues of the best immunosuppressant to be selected are under consideration. Decision on the use or withdrawal of immunosuppressant drugs requires careful review of the disease status, concomitant disease and other factors influencing the final outcome.

BACKGROUND

The era of kidney transplantation has begun on the 23rd of December 1954 in Boston, after successful procedure between identical twins performed by Joseph Murray. The transplant recipient survived for 9 years without immunosuppressive therapy and died of myocardial infarction. Successful transplantations among twins have prompted further attempts for such a treatment also among unrelated individuals. However, due to the immunological barrier the failure rate was high – the regular kidney transplantation programmed, also from unrelated donors, was initiated in 1954 after introduction of azathioprine and prednisolone to the immunosuppressive treatment.^{1–4}

In the next years, the understanding of the mechanisms of immunological response has led to the notable increase of pharmacological immunotherapy availability. Contemporary immune suppressive regimens have extended the mean transplant survival time in Poland to 8–10 years.^{4–6}

Clinicians remain fully aware of the adverse effects of the immunosuppressant treatment, operating on the principle of the lesser evil. With unproblematic and optimal transplant function the clinician often tends to be willing to reduce the immune suppression; however, in practice the fear against the transplant rejection is overwhelming this trend.

Transplantation between the closely related individuals, especially homozygous twins, seems to be a different issue in this context. Opinions on the immunosuppressive regimens in such cases tend to be extremely diverse.^{7–15}

In theory, transplantation between the homozygous twins does not require immunosuppressant; therefore drug toxicity might be avoided. However, it was noted that the risk of recurrence of the primary disease, which might have been treated with immune suppression is high.^{2–6} Moreover, it was observed that during the intrauterine fetus growth DNA mutation is often observed, resulting in

phenotypic and genotypic divergence even in homozygous twins.

These facts lead to the variety in opinions on the therapeutic approach in such cases. In this work we would like to describe the case of the transplantation in homozygous twins and related clinical dilemmas.

CASE PRESENTATION

In this report, we would like to present the case of 29-year-old male, Caucasian patient with stage 5 chronic kidney disease due to diarrhoea related haemolytic-uraemic syndrome (HUS) in the childhood (7th month of life, treated with temporary peritoneal dialysis for the duration of 3 months, however no recovery of the kidney function was noted). Despite seemingly atypical course of HUS, it is impossible to provide an alternative diagnosis at this stage. The patient was regularly dialysed since 1996 (starting at the age of 14), at first by peritoneal dialysis, then due to the recurrent peritonitis and loss of exchange efficacy, with haemodialysis. One year later (12th March 1997), the first kidney transplantation was performed with the organ harvested from the cadaveric donor (human leucocyte antigen (HLA) concordance – 14 points, kidney from 8-year-old male, Caucasian donor, PRA antibody activity – 0%). Haemodialysis was reintroduced after the graft function impairment (chronic graft nephropathy) in 2003. In kidney biopsy chronic vascular rejection was observed but the patient was not adherent to the immunosuppressive therapy, and graft nephrectomy was performed. Subsequent haemodialysis, despite every effort for maximum optimisation, was poorly tolerated by the patient. Difficulties with blood pressure normalisation, secondary hyperparathyroidism and concomitant osteopathy were observed. The patient underwent two surgeries of the pathological thoracic spine fractures and splenectomy due to spontaneous splenic rupture and bleeding.

The difficulty on the maintenance of the permanent vascular line for haemodialysis was notable. Several attempts to create the arteriovenous fistulae failed, with necessity to use carotid, subclavian and ultimately femoral venous catheters. A total of 10 units of red blood cells was transfused in the observation period after the first kidney transplantation.

After voluntary assent, the second kidney transplantation was performed with kidney harvested from the monozygotic twin, after confirmation of the full genetic concordance, on 26th October 2009. Prior to this procedure PRA activity was monitored closely, with increase to 50% after loss of the first graft and subsequent total loss of reactivity (0%) before the second transplantation. Anti-HLA antibody level was not monitored.

In the postsurgical period, the deep venous thrombosis (DVT) as well as urinary retention in the bladder related to the urethral stenosis were observed. After introduction of antibiotics and anticoagulants, distending of the urethra and all the above symptoms resolved. The patient was discharged after 21 days with excellent kidney function (copious diaeresis, serum creatinine levels of 0.72 mg/dl, glomerular filtration rate (GFR) – 137.5 ml/min) and has been regularly followed up ever since. The remaining kidney function in the donor is satisfactory as well, with transient increase in the blood pressure only and good renal function (creatinine – 1.2 mg/dl, GFR – 80 ml/min).

DISCUSSION

The immunosuppressive therapy in this case was challenging from the outset. The patient had been on kidney replacement treatment for 13 years in total (peritoneal and haemodialysis; two renal transplantations) with loss of vascular accessibility, and severe treatment complications (hyperparathyroidism and osteopathy necessitated urgent transplantation). The fact that DNA testing confirmed genotypic identity between the transplant donor and recipient favoured immunosuppressant withdrawal. On the other hand, possibility of the immunisation during the first transplantation and necessity to reduce the risk after the second procedure (high death rate associated with poor vascular access) prompted for cautious use of immunosuppressant.

Arguments for withdrawing from the immunosuppressive therapy are obvious and result from widely known side effects of these drugs (predisposition to infection, cancerogenic properties, diabetes, hyperlipaemia, hypertension, haematological alterations, bone diseases etc). If unnecessary, it should be stopped. However, almost never, despite full genetic identity the clinician is certain that the decision to withdraw the immunosuppressive therapy would not result in the transplanted kidney rejection. This is even more important in the case where the strict control of such patients by monitoring the biochemical parameters (GFR, indicators of inflammation), to assess the degree of immunisation (PRA), or a control biopsy of the kidney, could be helpful in the decision to withdraw the immunosuppressive therapy.

In the case presented, the patient received the reduced dose of steroids (methylprednisolone infusions – 250 mg intravenously once a day in 3 days with subsequent oral prednisone 20 mg daily in the decreasing doses) and mofetil mycophenolate 1 g twice daily. Due to the DVT

history occasional anticoagulant and antibiotic treatment was commenced. Further reduction of the immune suppression is currently being considered.

Reference data remain inconclusive in the respect of practical management of such a patient. Kessaris *et al*,⁸ in a large analysis of the outcome in 120 cases of kidney transplantation from twins in the USA and 12 in UK, performed from 1988 to 2004 have shown that the success rate in such procedures is high. In the USA 1 and 5-year transplant survival rates were 99.17% and 88.96%, respectively. However, in this study it is not clear if twin identity was always confirmed by DNA testing or was largely phenotype based. Moreover, comparative analysis of the treatment results in kidney transplanted twins on immune suppression (n=82) and without it (n=38) did not produce conclusive data (differences statistically insignificant p=0.12). In the 5-year follow-up in the group on immunosuppression, four individuals lost the kidney, and two died, while in the non-treated group five patients lost the graft and one died.

To sum up, the presented data do not allow to select the optimal treatment in the similar clinical situations. Individual consideration must include degree of genetic and immunologic concordance, concomitant disease, as well as additional factors influencing future outcome of the transplantation (age, gender, number of transplantation) with decision on the exact immunosuppressive regimen related also to the function of the transplanted kidney.

Learning points

- Even in case of the transplantation from the homozygous twin, selection of the immunosuppressive therapy, needs to be individualised taking into account: transplantation history, primary disease of the recipient and the degree of immunisation of the patient.
- The decision to discontinue immunosuppressive therapy is difficult with multiple factors to be considered: postoperative course, the nature of the underlying disease, the degree of immunisation and the current status of the graft (supported by an assessment biopsy).
- In case of immunosuppressive treatment discontinuation meticulous follow-up is required.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Pszenny A**, Gutowska D, Czerwiński J, *et al*. Long-term survival after kidney transplantation from homozygotic twin—a case report. *Ann Transplant* 2007;**12**:46–8.
2. **Simmons RL**, Van Hook EJ, Yunis EJ, *et al*. 100 sibling kidney transplants followed 2 to 7 ½ years: a multifactorial analysis. *Ann Surg* 1977;**185**:196–204.
3. **Bentley FR**, Sutherland DE, Fryd DS, *et al*. Similar renal allograft functional survival rates for kidneys from sibling donors matched for zero-versus-one haplotype with the recipient. *Transplantation* 1984;**38**:674–9.
4. **Krishnan N**, Buchanan PM, Dzebisashvili N, *et al*. Monozygotic transplantation: concerns and opportunities. *Am J Transplant* 2008;**8**:2343–51.
5. **Seigler HF**, Gunnells JC Jr, Robinson RR, *et al*. Renal transplantation between HLA-A identical donor-recipient pairs. Functional and morphological evaluation. *J Clin Invest* 1972;**51**:3200–15.

6. **Shimmura H**, Tanabe K, Ishida H, *et al*. Long-term results of living kidney transplantation from HLA-identical sibling donors under calcineurin inhibitor immunosuppression. *Int J Urol* 2006;**13**:502–8.
7. **Gumprich M**, Woeste G, Kohlhaw K, *et al*. Living related kidney transplantation between identical twins. *Transplant Proc* 2002;**34**:2205–6.
8. **Kessaris N**, Mukherjee D, Chandak P, *et al*. Renal transplantation in identical twins in United States and United Kingdom. *Transplantation* 2008;**86**: 572–7.
9. **Tilney NL**. Renal transplantation between identical twins: a review. *World J Surg* 1986;**10**:381–8.
10. **Sumrani N**, Delaney V, Ding ZK, *et al*. HLA-identical renal transplants: impact of cyclosporine on intermediate-term survival and renal function. *Am J Kidney Dis* 1990;**16**:417–22.
11. **Cheigh JS**, Chami J, Stenzel KH, *et al*. Renal transplantation between HLA identical siblings. Comparison with transplants from HLA semi-identical related donors. *N Engl J Med* 1977;**296**:1030–4.
12. **Kaufman DB**, Sutherland DE, Noreen H, *et al*. Renal transplantation between living-related sibling pairs matched for zero-HLA haplotypes. *Transplantation* 1989;**47**:113–19.
13. **de Mattos AM**, Bennett WM, Barry JM, *et al*. HLA-identical sibling renal transplantation—a 21-yr single-center experience. *Clin Transplant* 1999;**13**:158–67.
14. **Matas AJ**, Payne WD, Sutherland DE, *et al*. 2,500 living donor kidney transplants: a single-center experience. *Ann Surg* 2001;**234**:149–64.
15. **Kim YK**, Yoon HE, Kim SH, *et al*. Long-term follow-up of three identical twin transplant recipients without maintenance immunosuppressive therapy. *Nephrology* 2008;**13**:447–8.

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