Case Report: Let Us Not Forget the Treatment That Some Patients Have Received—The Brief 50-Year History of a Kidney Transplant Survivor

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Background: There has been a considerable improvement in post-transplant care since the early 1960s. Some patients we meet in the clinic have personally experienced this progress and have histories to tell that one must not forget. This is the brief history of a long-time “transplant survivor.”

Case Presentation: In 1970, a young woman developed acute oedema, proteinuria, hypertension and oliguria during pregnancy. Labor was induced, but neither the child nor the kidney function could be saved. Our patient started dialysis, and 4 years later received a kidney transplant donated by her father (then 55 years of age). Maintenance immunosuppression consisted of prednisolone and azathioprine until 2011, when azathioprine was switched to everolimus due to skin cancer. Before this, our patient was highly satisfied with prednisolone/azathioprine, despite discussions regarding newer immunosuppressive drugs, and always reminded the treating physician that one should “never change a winning team.” Retrospectively, the avoidance of calcineurin inhibitors might have been beneficial for this patient who still has preserved an excellent renal function with s-creatinine levels around 100 µmol/L and just had sparse fibrosis detected in a recently performed transplant biopsy. The transplanted kidney is now 101 years old and is still working 24/7.

Conclusions: Our patient received a kidney transplant for 46 years ago and still has a remarkably stable transplant function with s-creatinine levels around 100 µmol/L. This case report illustrates the potential endurance of the kidneys and is a reminder to keep taking individualized treatment decisions even though new treatment alternatives promise superiority.

Keywords: kidney, transplantation - kidney, biopsy, immunosuppressants, history
BACKGROUND

Recently, a 72-year-old Caucasian woman who has been followed at our unit for 50 years came for a regular outpatient visit. She developed renal failure in 1970 and received a kidney transplant in 1974. Her kidney transplant has been well-functioning ever since, despite 46 years’ treatment with immunosuppressive medication. In April 2020 when the kidney transplant had passed 101 years of age, a biopsy was taken (Figure 1), demonstrating only sparse fibrosis.

This is the brief history of a long-time transplant survivor.

CASE PRESENTATION

Our patients’ medical history started in 1970 when she was pregnant (para 1). At the end of the last trimester, she developed oedema and proteinuria without signs of hypertension earlier during the pregnancy. Six days before the estimated time of delivery, she developed severe vaginal bleedings, hypertension (150/130 mmHg), proteinuria (2 g/24 h), oedema and eventually oliguria. Placental bleeding was suspected leading to an emergency induced labor, which resulted in stillbirth. Post-delivery blood pressure stabilized without antihypertensive treatment, but oliguria persisted and eventually our patient became anuric, thus peritoneal dialysis was started.

As the clinical presentation was considered atypical for pregnancy-related kidney disease, it was decided to perform a kidney biopsy. After the first attempt with a blindly sampled percutaneous procedure not obtaining any representative material, an open biopsy procedure was chosen for the second attempt. The pathologists described generalized cortical necrosis in the kidney biopsies, thought to be caused by severe pre-eclampsia. Urine production gradually increased and dialysis could be halted after about 5 weeks. After cessation of dialysis, renal function was stable with creatinine clearance levels around 15–16 ml/min and proteinuria 1.1 g/24 h. Blood pressure levels remained elevated at 160–180/100–110 mmHg, but no antihypertensive treatment was started. At a routine consultation in October 1973, the treating physician described her as “wellbeing” even though hemoglobin level of 4.7 g/dl and s-creatinine at 1122 µmol/L (12.7 mg/dl) was remarked. Our patient was informed to start oral iron supplementation and that . . . .

Subsequently, pre-transplant work-up was initiated what included evaluation of family members as potential donors. The father of our patient (then aged 55) was accepted as donor and the transplantation was scheduled for January 1974. An accidental bleeding during the transplant procedure led to a per-operative splenectomy. Total cold ischemia time of 44 min was registered for the kidney transplant and 3,000 ml infusion fluids were given to the transplant recipient together with 300 mg hydrocortisone and 175 mg azathioprine as initial immunosuppression.

A clinical rejection was suspected on post-transplant day 6 due to an increase in s-creatinine- from 106 µmol/L (1.2 mg/dl) to 150 µmol/L (1.7 mg/dl). Anti-rejection treatment consisting of 5 gram intravenous methylprednisolone and radiation therapy [150 Roentgen × 3 (equivalent to 1.5 Gy × 3)] was started.
without histological verification of the rejection diagnosis. Renal function stabilized [creatinine 115 µmol/L (1.3 mg/dl)] after the rejection episode and the patient was discharged at day 12 with the following daily medication: prednisolone 50 mg q.d., azathioprine 175 mg q.d., furosemide 40 mg t.d.s. and no anti-hypertensive treatment.

At the clinical visit at 1 year after transplantation she reported to be very well. The clinician noted cushingoid characteristics, 124/60 mmHg blood pressure and creatinine clearance 93 ml/min. Our patient was informed to continue following medication: prednisolone 175 mg q.d., azathioprine 225 mg q.d and furosemide 40 mg q.d, in addition to iron supplements and antacids. Eighteen months after transplantation the prednisolone dose was tapered to 10 mg q.d. and azathioprine dose to 100 mg q.d.

The following years went without any specific concerns. Renal function remained stable with serum creatinine values around 105 µmol/L (1.3 mg/dl).

From 15 years on after transplantation a broad specter of skin manifestations was diagnosed and treated: solar keratosis, fibroepithelial polyps, seborrheic keratosis, nodular basal cell carcinoma and squamous cell carcinoma. The different skin lesions slowly improved after azathioprine was switched to everolimus, an inhibitor of the mammalian target of rapamycin (mTORi) in 2011 (trough 4–8 µg). After the drug switch, serum cholesterol levels increased, followed by intensified lipid-lowering therapy. In 2017, she developed symptoms of angina pectoris. Coronary angiography revealed left coronary artery stenosis and a drug eluting stent was successfully implanted. Bone density has been measured regularly. The first signs of osteopenia were registered in 1998 and regional osteoporosis was diagnosed in 2019.

In April 2020, her blood pressure was 124/60 mmHg and serum creatinine value was 113 µmol/L. Current medication consisted of prednisolone 5 mg × 1, Everolimus 1 mg × 2, acetylsalicylic acid 75 mg × 1, rosvastatin 10 mg, ezetimib 10 mg, in addition to a combination of calcium and vitamin D at 1,000 mg/800 units.

DISCUSSION

This patient is a living witness of modern nephrology history. Hemoglobin levels below 5 g/dl due to renal anemia was treated with blood-transfusions and iron supplements in the 1960–70s; recombinant erythropoietin arrived on the market in the late 1980s (3). Blood access for receiving haemodialysis prior to transplantation was achieved through an indwelling shunt placed externally on the forehead (Figure 2). The first kidney transplantation in Norway was performed in 1956, but the official transplant program was only 6 years old when our patient was transplanted in 1974.

Short and long-term outcome following kidney transplantation in the 70s was poor. One-year rejection rates were 70%—80% while the 1- and 5-year patient survival was 60 and 45%, respectively (4). In 1974, the pre-transplant immunological testing was restricted to HLA-A and HLA-B phenotyping in addition to cross-matching, and mismatches
inhibitors might have been beneficial for our patient to preserve function when combined with mycophenolate mofetil and corticosteroids after renal transplantation (19, 20). A tacrolimus-based immunosuppressive regime was given to over 90% of new adult kidney transplant recipients in the United States in 2020 (21). CNI-free protocols after renal transplantation are available, which includes mTOR-inhibitors (22) or belatacept (23) but often lead to more rejections.

Our patient did, however, switch from azathioprine to everolimus in 2011 after being treated for several skin cancers, as the mTORs then had demonstrated a possible reduced risk for skin cancer (24).

After this switch, a severe worsening of her blood lipid profile was registered, a well-known side-effect of everolimus (25). Fluvastatin was initiated in order to reduce the cardiovascular risk (26) and later replaced with rosuvastatin (27). Despite these preventive efforts, our patient developed symptomatic angina, which was efficiently treated with percutaneous coronary intervention in 2017.

This kidney transplant has been through 101 rough years, but still there is only sparse fibrosis in the recent transplant biopsy which by our pathology unit was evaluated as a normal kidney transplant biopsy according to the Banff classification: The s-creatinine remains at levels around 100 µmol/L (1.1 g/dl) and just sparse proteinuria has been registered. It is out of the range for this report to answer how old a transplanted kidney can get, but we do think this case illustrates which endurance the kidneys might have but also that the expression "never change a winning team" might be relevant in the navigation of different immunosuppressive regimens in the follow-up of kidney transplant recipients.

The story doesn’t end here but goes on and just like in the fairytales… the patient and her transplanted kidney lived happily ever after…. 

**DATA AVAILABILITY STATEMENT**

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

**ETHICS STATEMENT**

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

**AUTHOR CONTRIBUTIONS**

EN, MR, and KM created the idea and reviewed and finished the manuscript. EN drafted the manuscript. All authors have read and approved the manuscript.

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