Clinical Case Studies and Reports

Case Report

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Refractory hypotension in an anephric patient: Immediate response to renal transplantation

"I have my life back...without transplantation I did not have a quality of life...Other than for dialysis, I would not go outside for months at a time." 64 yo patient, 8 years post-transplant.

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Abstract

A 57 yo woman underwent bilateral nephrectomy for autosomal dominant adult polycystic disease with massive organ enlargement. Despite severe pre-operative hypertension, her postoperative course was complicated by very severe debilitating hypotension, especially on dialysis, and refractory to multiple attempted interventions. Carefully planned deceased donor renal transplantation resulted in immediate post-operative normalisation of blood pressure, sustained improvement to quality of life and excellent graft function eight years later.

Background

Autosomal dominant polycystic kidney disease (ADPCKD) is an inherited progressive, multisystem disorder characterised by innumerable renal cysts, hepatic cysts and occasionally, cerebral aneurysms. Cysts become symptomatic from the 2nd decade, and patients are generally dialysis dependent between the 4th and 7th decade [1]. Complications of ADPCKD include treatment-resistant hypertension, renal cyst rupture with haematuria, recurrent intra-abdominal infections, renal calculi, dyspepsia, early satiety and chronic abdominal pain [2]. Nephrectomy may be required in the setting of massive nephromegaly, especially if renal transplantation is planned. Chronic hypotension may follow bilateral nephrectomy. This is incompletely understood, although multiple mechanisms including vasoactive mediators, circulating blood volume and hyporeninemia are important [3-5]. Intradialytic hypotension causes headache muscle cramps, inadequate dialysis, fistula thrombosis, recurrent syncope, orthostatic hypotension and fatigue [6]. These complications impact heavily on quality of life. Renal transplantation carries additional morbidity and mortality risks due to ischemic organ damage, and affected patients may be excluded from transplantation.

Case presentation

The diagnosis of ADPCKD followed presentation with acute subarachnoid haemorrhage at age 23, due to spontaneous rupture of an anterior cerebral artery aneurysm. Hypertension was treated, but progressive renal impairment supervened by age 40. Haemodialysis via arteriovenous fistula was initiated at age 57, when her kidneys had enlarged to the point of continuous discomfort and malnutrition. She commenced haemodialysis and underwent uncomplicated bilateral nephrectomy, at which her cystic kidneys weighed 13.7 kg. In the subsequent 18 months, the patient suffered persistent symptomatic hypotension with daily pre-syncopal or syncopal episodes resulting in multiple presentations to hospital and a fall with a tibial plateau fracture. There were problematic dialysis sessions including headaches, muscle cramps and syncope. Extensive investigations were negative, and interventions including volume expansion, long dialysis with low blood flow, sodium profiling, prednisolone, fludrocortisone, cautious salt supplementation and midodrine produced no or minimal improvement. Compliance with fluid restriction was excellent, with interdialytic weight gains usually 1.5-2 kg. Testing for adrenal insufficiency was negative, and no adrenal tissue was identified in the nephrectomy specimens. Echocardiography demonstrated normal cardiac function.

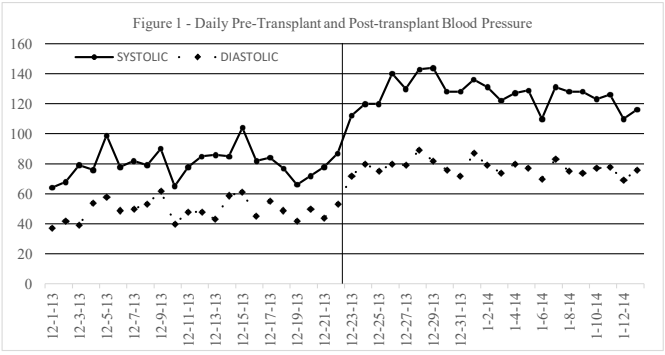

Figure 1. Daily averaged blood pressures in the 21 days prior to transplant and 21 days post-transplant. The vertical line represents 22/12/2012, the date of renal transplantation. A sustained rise in both systolic and diastolic blood pressure can be seen immediately post-transplantation

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The patient was unable to work, essentially bedbound between dialysis sessions. She was constantly hypotensive even when oedematous, and postural hypotension induced frequent syncope, often requiring transfer to the Emergency department from a truncated dialysis session. She had poor quality of life despite a supportive home situation, positive outlook and high educational achievement.

The perioperative risks were initially assessed as precluding renal transplantation, due to profound hypotension and multi-organ ischaemic injury. However, given poor quality of life and inability to effectively dialyse, a multidisciplinary team, including the fully-informed patient and her partner, planned deceased donor transplantation with post-operative intensive care.

Pre-operative serum creatinine was 885 mmol/L, and blood pressure 87/53 mmHg. Intra-operatively, the patient was given three liters intravenous fluid, metaraminol and ephredine boluses to maintain mean arterial pressure.

Immediate post-operative blood pressure was consistently over 100/70 mmHg, without vasopressor requirement. She received standard immunosuppression. Graft function was immediate, with serum creatinine reducing to 69 mmol/L on day 3. She was discharged home day 6 with creatinine 58 mmol/L and blood pressure 144/82 mmHg. Blood pressure is now typically 120/75 mmHg; baseline creatinine is approximately 60 mmol/L. The patient makes approximately 1.5 L of urine daily and has no fluid restriction and has no symptoms of hypotension. She remains well, fully engaged in all aspects of normal life.

Discussion

Bilateral nephrectomy remains a treatment option in the management of end-stage polycystic kidney disease. Among the indications is malignant hypertension, recurrent abdominal infection and to mitigate the disabling consequences of massive organomegaly. In some anephric patients, chronic symptomatic hypotension occurs following surgery. The mechanism of this hypotension has not been fully elucidated, though alterations in the renin-angiotensin axis and endogenous vasoactive mediators are thought to play a central role. In a longitudinal case series, Liu, *et al.* evaluated the circulating renin-angiotensin system (RAS) of four anephric patients using serial radioimmunoassay [7]. Two patients became hypotensive following nephrectomy; one recovered after six years, the other had not recovered at publication. All four patients demonstrated abnormally low plasma renin levels, but normal plasma angiotensin II and aldosterone. The authors concluded despite an absent renin state, kidney-independent mechanisms of angiotensin II compensated for long term blood pressure. Although limited by sample size, this study postulates alteration of the RAS axis results in hypotension following nephrectomy. The authors did not comment on the mechanism for hypotension in two patients despite comparable RAS assays over eight years. Cases, *et al.* identified adrenomedullin, a nitric oxide vasodilator, significantly elevated in hypotensive dialysis patients compared with matched normotensive controls, suggesting the role of endogenous vasoactive mediators in the renal failure population [5].

A number of case studies report a beneficial effect of transplantation on quality of life for hypotensive dialysis patients. Sun, *et al.* describes the case of a 57-year old female on dialysis for six years due to diabetic nephropathy, complicated by chronic symptomatic hypotension despite mineralocorticoids and alpha agonist therapy [8]. The patient underwent living-related donor transplantation, with normalisation of her blood pressure on day 1 post-operatively, and adequate graft function at 3 weeks.

In a single centre study of 33 patients, Bellini, *et al.* found bilateral native nephrectomy for ADPKD to be safe regardless of transplantation status, with an overall mortality of 3% [9]. 15 patients were dialysis-dependent pre-operatively, 18 patients were post transplantation. The study did not comment on perioperative blood pressure or symptoms of hypotension.

Muscroft, *et al.* found in eight cases of dialysis-dependent patients with symptomatic hypotension, transplantation normalised blood pressure [10]. In this study, all patients required vasopressors post-transplant in intensive care settings, but as graft function improved and vasopressors weaned, normotension was maintained. One eight transplant patient died due to ischaemic bowel post-operatively.

Ignacak, *et al.* presents the case of a 44-year old female post-bilateral nephrectomy for infected kidneys, with end-stage renal failure due to a rapidly progressing glomerulonephritis [11]. The patient underwent renal transplantation after three years of dialysis complicated by intra-dialytic hypotension. Transplantation was initially complicated by delayed graft function, but the patient had excellent graft function at one year follow up.

Timing of renal transplantation in dialysis-dependent polycystic kidney disease is an emerging interest area. Case series suggest the perioperative morbidity is unchanged between concomitant and staged nephrectomy and transplantation. Glassman, *et al.* found no significant differences in morbidity or mortality in a small case-matched study of ten patients undergoing concomitant bilateral nephrectomy and transplantation versus a group of nine patients undergoing staged nephrectomy and transplantation [12]. In a study of one hundred ADPCKD patients stratified to simultaneous ipsilateral nephrectomy and transplantation or transplantation without nephrectomy, Neef, *et al.* found no peri-operative outcome difference, an overall surgical complication rate of 12% and patient survival at 5 years of 93% [13]. Pre-nephrectomy transplantation may be extremely difficult in the presence of existing grossly enlarged kidneys. However, if safe and efficacious, concomitant transplantation may prevent chronic hypotension and ameliorate the impact on quality of life of hypotensive dialysis.

Conclusion

This case illustrates the transformative effect of transplantation in a 57-year old woman after bilateral nephrectomy for massive polycystic kidneys. Dialysis was tolerated very poorly due to hypotension, and transplantation was relatively contraindicated due to high peri-operative mortality and morbidity. However, blood pressure normalised immediately following transplantation, with excellent graft function and substantial improvement in quality of life eight years later.

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