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CASE REPORT

# Paradoxical increase in blood pressure following bilateral native nephrectomy

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### Key Clinical Message

Hypertension with Chronic kidney disease is often difficult to control medically. In such patients, nephrectomy can help to control blood pressure (BP). We describe a case of a 6-year-old boy with autosomal recessive polycystic kidney disease who showed a paradoxical increase in BP following bilateral nephrectomy.

### Keywords

Bilateral nephrectomy, hypertension, polycystic kidney disease.

## Introduction

Hypertension is commonly observed in the pediatric population [1]. Moreover, it is a well-known cause of morbidity and mortality in children [2]. Pediatric hypertension is most commonly renal in origin and is caused by either parenchymal disease or by renal artery stenosis [3]. Although medical treatment is the first-line therapy for this condition, it may occasionally fail to control blood pressure (BP). Some patients with renal hypertension due to chronic kidney disease (CKD) are resistant to antihypertensive medications and even to aggressive dialysis aimed at achieving ideal body volume control [4]. In such patients, unilateral [5] or bilateral native nephrectomy [6, 7] may be successful in controlling BP. Previous studies have reported that patients may have a partial or a poor response to surgery [4, 8, 9], whereas others have reported a delay in response of up to 6 months after surgery [5, 10]. Postoperative volume-mediated hypertension has been reported in patients with autosomal recessive polycystic kidney disease (ARPKD) and in those with focal segmental glomerulosclerosis (FSGS), although these patients were managed successfully with intensified dialysis [11]. However, no studies have reported a failure of treatment accompanied by a paradoxical increase in BP after nephrectomy, that is, BP levels that are higher than preoperative baseline levels.

Although a previous study has indicated that preoperative hypertension-related signs and symptoms are significantly associated with the response to nephrectomy [12], there's limited evidence of predictors of a successful response to surgery.

In the present report, we describe a case of a 6-year-old boy with ARPKD who experienced a paradoxical increase in BP following bilateral native nephrectomy. The increase in BP failed to respond postoperatively despite the administration of 6 antihypertensive agents as well as intensive hemodialysis to avoid volume-related hypertension.

## Case Report

A 6-year-old boy presented with acute respiratory infection. He was known to have end-stage renal disease secondary to ARPKD with associated hypertension, along with a history of closed patent ductus arteriosus (PDA),

bronchial asthma, and global developmental delay. His parents were first-degree cousins, and he had one similarly affected sibling who had died immediately after birth. Both parents were screened for renal cysts through ultrasonography and both had normal kidneys with no cysts. The patient's condition was diagnosed antenatally, following the diagnosis of maternal oligohydramnios. He was born at 33 weeks' gestation and weighed 2.07 kg. However, he required admission to the neonatal intensive care unit (NICU) due to complications arising from pulmonary hypoplasia. Postnatal abdominal ultrasonography showed bilateral, hyperechoic, enlarged kidneys, suggesting the presence of bilateral polycystic kidney disease. Radioisotope renography with Tc99m-mercaptoacetyltriglycine indicated marked functional renal impairment. He showed normal results on a micturating cystogram. The patient had not been tested genetically because the test is not available in our country. Moreover, the diagnostic criteria of ARPKD don't necessitate genetic testing to confirm the diagnosis [13].

During his NICU stay, the patient became hypertensive and was managed with oral nifedipine, hydralazine, and propranolol. Thereafter, the patient was maintained on CKD medications in the form of ferrous sulfate, sodium resonium, alfacalcidol, epoetin alfa, and sodium bicarbonate in addition to antihypertensive medications. The patient's BP remained uncontrolled, and the readings were higher than the 95th percentile for his age, sex, and height.

The patient first presented at our hospital at the age of 6 years with a respiratory infection. His blood pressure was 189/71 mmHg. He was found to have end stage kidney disease (ESKD) (creatinine, 848 [range, 28–56] $\mu$mol/L; urea, 33.9 [range, 1.8–6.5] mmol/L; GFR: 4.5 [range, 133.0 $\pm$ 27.0] mL/min/1.73). Sodium and other electrolytes were normal and the patient didn't require any sodium supplementation. A complete blood count indicated the presence of thrombocytopenia and microcytic hypochromic anemia (platelets, 65,000 [range, 150,000–400,000]/mm$^3$; hemoglobin, 8.8 [range, 10.2–15.2] g/dL). The patient's hypertension was initially managed with a labetalol infusion; 10 mg oral enalapril, once a day [OD]; 25 mg hydralazine, three times a day [TID]; and 0.25 mg prazosin, TID; were subsequently added. Abdominal ultrasonography showed severe hepatosplenomegaly; the liver was 13.4 cm in size and exhibited periportal thickening, while the spleen was 12 cm in size. Furthermore, the kidneys were replaced with variable cysts, and the cortices were echogenic. Doppler ultrasonography and upper gastrointestinal endoscopy were unremarkable. A biopsy of the liver showed hepatic fibrosis. The patient's BP was difficult to control and remained in the range of 130/70–178/92 mmHg, average readings were initially 136/84, 144/82, and 158/88 mmHg, despite the administration of the maximum doses of six antihypertensive medications (10 mg amlodipine, OD; 25 mg hydralazine, TID; 5 mg lisinopril, OD; 0.5 mg prazosin, TID; 12 mg furosemide, TID; and 2.5 mg nifedipine PRN).

Doppler echocardiography revealed left ventricular hypertrophy but normal cardiac function (ejection fraction, 65%). There was no coarctation of the aorta. Despite a urine output of 5 mL/kg/h and despite including eight antihypertensive agents (3 mg/kg/h labetalol; 10 mg amlodipine, OD; 2 mg prazosin, TID; 25 mg hydralazine, TID; 25 mg atenolol, OD; 7.5 mg lisinopril, OD; 45 mg methyldopa, TID; and 12 mg/12 h furosemide) in the patient's medications, he remained hypertensive, average readings were 159/90, 176/113, 196/109, and 201/123 mmHg for 6 days. Therefore, bilateral native nephrectomy was performed along with splenectomy and peritoneal dialysis catheter insertion. His BP was maintained intraoperatively at approximately 100/55 mmHg, and on the first post-operative day, it was approximately 110/80 mmHg without any medications. He had no immediate postoperative complications.

On the second postoperative day, the patient became hypertensive (BP, 152/89 mmHg). He did not have signs of fluid overload. Twenty five milligram Labetalol, OD and 2.5 mg mg hydralazine, every 6 h [Q6] were restarted. Five milligram amlodipine was added in the next day and the patient was transferred to the pediatric ICU. His arterial blood gas showed a picture of persistent metabolic acidosis along with persistent hyperkalemia in his lab tests and hence, hemodialysis was started. The child was maintained at the target dry weight through regular hemodialysis sessions (3–4 times/week). Dry body weight was determined during hemodialysis session as the lowest weight a patient can tolerate without the development of symptoms or hypotension. However, from the 18th postoperative day, his BP was progressively increasing from 193/111 to 201/95 and even to 231/155 mmHg. His average readings were 193/123, 200/112, and 213/126 mmHg. His blood pressure didn't show any improvement following dialysis sessions. Thyroid function tests were normal, and an iodine-131-meta-iodobenzylguanidine (MIBG) scan was also normal; thus, the remote likelihood of a pheochromocytoma was excluded. Serum catecholamines weren't measured because they are not available at our hospital and they are not superior to MIBG. A repeat abdominal ultrasonography showed increased hepatic echotexture with mild intrahepatic biliary duct dilatation and moderate free fluid. Peritoneal dialysis was initiated at 6 weeks after nephrectomy; the fill volume was gradually increased, and the patient was discharged on continuous ambulatory peritoneal dialysis (CAPD). At discharge, the patient was in a generally

stable condition with the exception of the persistent hypertension. His medications included amlodipine 5 mg OD, prazosin 1.5 mg TID, enalapril 10 mg OD, labetalol 50 mg TID, hydralazine 25 mg TID, and nifedipine 2.5 mg, 2.5 mg every 6 h as required, in addition to the CKD medications.

Although the patient's BP showed gradual improvement at 3 months after surgery, he remained hypertensive, with a BP of between 130/90 and 150/90 mmHg, and with intervals of higher readings (189/122 mmHg), although he was receiving the maximum possible doses of amlodipine, 5 mg OD; prazosin, 1.5 mg OD; enalapril, 10 mg OD, and hydralazine, 25 mg TID. At 6 months, his blood pressure became 110/60 mmHg on the same regimen except for amolidipine. He was also converted to hemodialysis. At 10 months, his blood pressure was 120/80 mmHg, on hydralazine 25 mg TID and Enalapril 10 mg OD. The child has been placed on the waiting list for kidney and liver transplants but he died 10 months after nephrectomy.

## Discussion

Hypertension is common in patients with CKD and may be caused by fluid overload or by increased renin secretion. The renin-angiotensin system is believed to be the key regulator of BP in patients with ARPKD, and it is believed to account for the hypertension observed among these patients [14, 15]. In the present case, adequate urine output was noted without any signs of fluid overload. Therefore, we assume that the hypertension was renin-mediated. In such patients in whom medical therapy has failed to control hypertension, bilateral nephrectomy is considered to be an appropriate surgical approach for normalizing BP

**Table 1.** Summary of Pediatrics and adults studies about the effect of bilateral native nephrectomy on controlling high blood pressure.

| Study | Type of study | Number of patients | Operation performed | Main results |
|---|---|---|---|---|
| Sharbaf et al., 2012 [11] | Cohort, retrospective | A total of 49 patients had bilateral nephrectomy for different reasons, 2 of which had the surgery for resistant hypertension | Bilateral native nephrectomy | Improvement in blood pressure was noted in both patients with reduction in antihypertensive medications requirement from 4 to 2 and from 2 to 0 respectively. Five patients with FSGS ($n$ = 4) and ARPKD ($n$ = 1) who had done nephrectomy for other causes had immediate postoperative hypertension which was managed successfully with immediate intensified dialysis |
| Gawish, 2010 [10] | Cohort, retrospective | A total of 28 patients had bilateral nephrectomy for different reasons, 19 of which had the surgery for resistant hypertension | Bilateral native nephrectomy | Hypertension started to show partial improvement at 3 months. Number of antihypertensive medications was reduced from 3.6 $\pm$ 1.05 to 2.69 $\pm$ 0.94. This effect was constant for 1 year. Significant difference was only noted at 3 years after surgery. The number of antihypertensive drugs was reduced to 1.46 $\pm$ 1.33 ($P$ = 0.008) |
| Baez-Trinidad, 2003 [9] | Cohort, retrospective | A total of 320 patients had nephrectomy (unilateral or bilateral) for different reasons, 8 of which had bilateral nephrectomy for resistant hypertension with long term follow up | Bilateral native nephrectomy | After a mean follow up period of 4.4 years, normalization of blood pressure was experienced by 7 patients. Five patients (63%) had normalization of blood pressure without any antihypertensive medications (complete success), two patients (25%) had normalization with reduced number of drugs from 4 to 1 and from 3 to 2 respectively. one patient (12%) failed to respond to treatment. He also had increased antihypertensive medications requirement |
| Macsim et al., 2012 [7] | Case report | One patient | Bilateral native nephrectomy | Patient showed tremendous response immediately after nephrectomy with reduction of antihypertensive medications from 7 to 4 at 6 months postnephrectomy |

 

[16]. Plasma renin levels are not routinely measured prior to bilateral nephrectomy, and therefore, the patient's renin level was not measured preoperatively, particularly because this test was not performed at our laboratories. Even if the test had been performed, the result would not have affected our decision to perform nephrectomy. It has previously been shown that intrarenal renin, rather than systemic renin, may be associated with hypertension in ARPKD patients [14, 15]. Furthermore, the plasma renin levels may be normal in children with ARPKD, as shown by a retrospective study describing the clinical features of 55 children with ARPKD [17]. In these children, plasma renin levels were found to be either low or normal, although 65% of cases had hypertension, suggesting that plasma renin is not involved in the pathway of hypertension in this population. A review of the literature indicated that a majority of the studies have shown significant improvement in BP following nephrectomy (Table 1). Although a delayed response has previously been reported, the normalization of BP eventually occurs, either completely, such that antihypertensive medications can be discontinued, or partially, such that the number of antihypertensive medications administered can be reduced compared to those required preoperatively. However, Increase in blood pressure following bilateral nephrectomy for causes other than the hypertension has been reported among dialysis-dependent patients who were previously normotensive, but this can be explained by the fact that these patients were already dialysis dependent and the increase in blood pressure is likely due to the loss of the residual salt and water excretion from the removed kidneys [18].

In the present case, bilateral native nephrectomy was associated with a significant increase in the patient's BP following a transient improvement, despite intensified volume control through dialysis. This transient postoperative improvement may have been related to the side-effects of anesthesia. Although previous studies have reported a link between splenectomy and pulmonary hypertension, [19] no association has been found between splenectomy and systemic hypertension.

Two months after bilateral nephrectomy, the patient's BP showed partial improvement, although the high readings necessitated the regular use of 5 antihypertensive medications. When we attempted to decrease the doses of these medications, his BP increased immediately. Thus far, we have been unable to elucidate the reason for this paradoxical increase in BP and the absence of a response to bilateral nephrectomy. Further research aimed at understanding the pathophysiology of hypertension in children with CKD will be required to optimize the management of these children. In addition, the short- and long-term outcomes of bilateral nephrectomy in patients with ARPKD should be assessed further.

## Conclusion

Based on the findings of the present case, we conclude that bilateral nephrectomy does not always yield an improvement in BP in children with ARPKD.

## Conflict of Interest

None declared.

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