CKJ

Clinical Report

Hypertension and a missing kidney

Rupesh Raina[1], Vikas Gulani[2], Lina Mehta[2], Gretta H. Jacobs[3], Kelly Joyce[4], Todd A. Ponsky[5] and David N. Kenagy[6]

[1]Division of Pediatric Nephrology, Department of Pediatrics, University Hospitals of Cleveland, Cleveland OH, USA, [2]Department of Radiology, University Hospitals of Cleveland, Cleveland, OH, USA, [3]Department of Pathology, University Hospitals of Cleveland, Cleveland, OH, USA, [4]Department of Pediatrics, University Hospitals of Cleveland, Cleveland, OH, USA, [5]Department of Surgery, University Hospitals of Cleveland, Cleveland, OH, USA and [6]Division of Pediatric Nephrology, Department of Pediatrics, University of Louisville, KY, USA

Correspondence and offprint requests to: David N. Kenagy; E-mail: david.kenagy@uhhospitals.org

Abstract
Standard initial assessment via ultrasound of a 4-year-old girl with hypertension revealed the absence of one kidney. Instead of cross-sectional imaging of the retroperitoneal space, a functional (nuclear) study was performed. This revealed a malformed kidney within the chest. Though systemic levels of renin and aldosterone were not elevated, removal of the malformed kidney normalized the blood pressure. The presence of prominent smooth muscle nodules surrounding the arteries was seen in the malformed kidney. Initial attempts to avert surgery by pharmacologically reducing blood flow to the malformed kidney were unsuccessful. The review of the literature offers little evidence to support such a strategy.

Keywords: congenital anomaly; ectopic kidney; hypertension; renovascular

Introduction

Hypertension in children may be due to renal or renovascular causes. Tullus et al. [1] recently published an algorithm for the orderly investigation of renovascular hypertension in children, in which ultrasonography is one of the primary studies. Ultrasound may reveal asymmetry of renal size suggestive of scarring. Doppler ultrasound non-invasively assesses renal artery flow, but is less sensitive than angiography. Computed tomographic (CT) angiography and magnetic resonance angiography (MRA) offer intermediate sensitivity. Digital subtraction angiography is the gold standard investigation for renovascular causes. In some children, hypertension accompanies congenital renal anomalies or an ectopic renal position. In some reports, magnetic resonance imaging (MRI) or retrograde pyelography led to the diagnosis when ultrasound failed to do so [2, 3].

The prenatal events that lead to renal ectopia are not known. When ectopia does occur, the thorax is an unusual location to find the kidney. Hahn et al. [4] described an intrathoracic kidney and postulated that contact with the diaphragm was the direct cause of malformation of the diaphragm. The obstruction of urinary drainage is believed to cause dysplasia and is associated with well-described pathological findings. Obstruction, however, is not believed to play a role in ectopia; yet, malformations often accompany ectopia.

Here, we report a child with hypertension and a malformed kidney in an unexpected location. We describe the use of new modalities for imaging and surgical correction, as well as pathologic findings that have not previously been described in this context.

Case report

A 4-year-old girl's pediatrician detected hypertension at a health supervision visit. The pressure was 112/78 (auscultated with a manual cuff). The 95th percentile pressure for her height and age were 108/70 [5]. Over the next few weeks, auscultated pressures ranged between 108–128 mmHg (systolic) and 76–88 mmHg (diastolic).

She had been born at 39 weeks to a 26-year-old G_3P_0 mother. Her mother had a bicornuate, septate uterus. The first pregnancy was ectopic. The second, a twin gestation, was terminated at 17 weeks due to neural tube defects in both fetuses and cardiac anomalies in one of them. To treat a hypercoagulable state during this and a fourth pregnancy, the mother received low-molecular-weight heparin and aspirin.

Prenatal ultrasounds were normal at 13, 17, 20 and 34 weeks. Growth and development were normal, with a height and weight at the 50th percentile.

Peripheral renin activity was 3.5 ng/mL/h (<15 ng/mL/h). Aldosterone was 31.4 ng/dL (range 4–76). Serum electrolytes were normal and creatinine was 0.43 mg/dL. The

complete blood count, thyroid stimulating hormone levels and T4 were normal. Her urine-specific gravity was 1.010, pH 7, with no heme, protein, nitrite or glucose. Urine microscopy revealed rare leukocytes without red cells. A urine culture was sterile.

A renal ultrasound revealed the left kidney to be 8.1 cm in length (between the 50th and 95th percentiles) [6]. No right kidney was detected. A nuclear renal scan demonstrated the normal uptake of nucleotide within the left kidney (Figure 1). There was no nuclear activity in the right renal fossa. However, synchronous with activity in the left kidney, a focus of abnormal activity appeared superiorly in either the lower aspect of the right hemithorax or the uppermost aspect of the abdomen.

To determine the location of the right renal remnants, MRI was performed. Figure 2 shows the relationship of the kidney to the surrounding structures. Figure 3 shows an aneurysm of the renal artery. Though displacement of the ectopic kidney and bowel into the thorax was noted, imaging did not clarify whether a Bochdalek hernia existed or an eventration of the hemidiaphragm.

Echocardiography revealed dilation of the aortic root and ascending aorta, with a small patent ductus arteriosus. Left ventricular mass/height was 41.8 g/m^2 (normal 19.4–38.6). There was no aortic coarctation.

Over a 4-month period, pharmacologic management was attempted. Enalapril was begun at 0.08 mg/kg and gradually increased to 0.35 mg/kg, while monitoring serum electrolytes and creatinine. Noting no change in blood pressures (118–122 mmHg systolic), the patient began losartan, which was increased gradually from 0.9 to 1.8 mg/kg. Enalapril was discontinued due to sleepiness, resolving this symptom. Though pressures improved
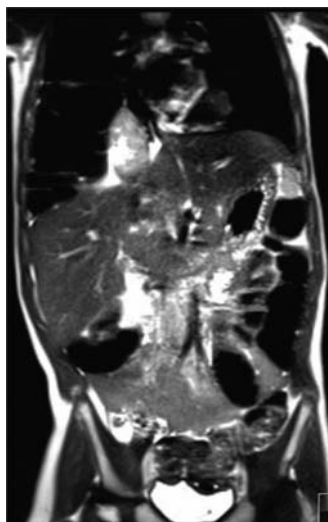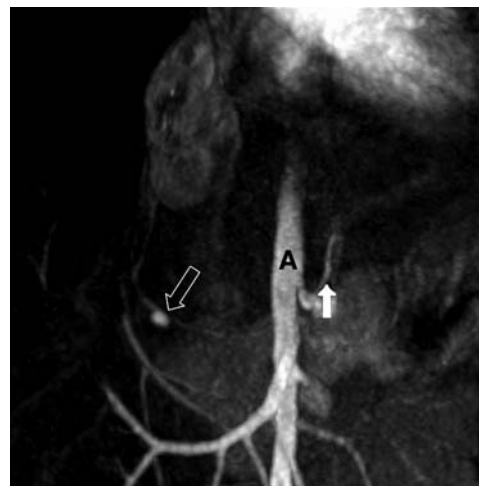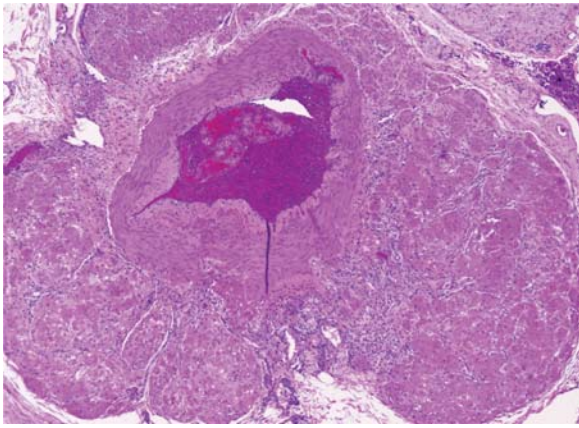

Fig. 3. Subvolume maximum intensity projection image from a single arterial phase frame. A small right renal artery (solid arrow) arises from the aorta (A), coursing first laterally, then cranially. An aneurysm (open arrow) is seen near the upward inflection of the vessel.

somewhat (average systolic pressure of 115 mmHg), she still did not maintain pressures below the 90th percentile (104 mmHg). Amlodipine was begun and titrated up to 0.5 mg/kg/day. Though the patient remained asymptomatic, it appeared unlikely that pressures could be normalized on a simple regimen without adverse effects. It was determined to remove the ectopic kidney. Pulmonary function testing demonstrated a near-normal forced vital capacity of 92%.
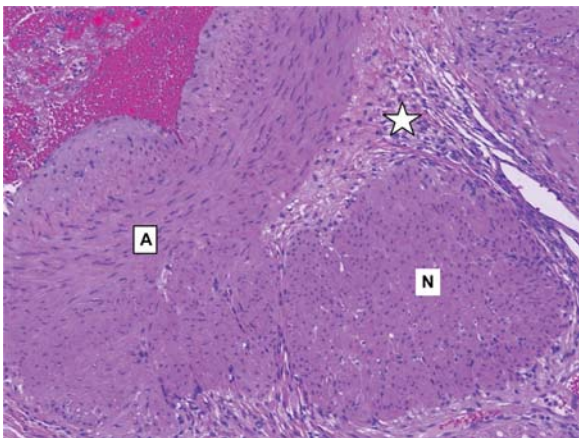
Laparoscopic nephrectomy was performed by a pediatric surgeon and an adult urologist. They found the kidney to be malrotated, with the hilum facing laterally. A right-sided diaphragmatic eventration was present with a very thin connective tissue sac that functioned as an elevated diaphragm, keeping the abdominal contents separate from the chest. Almost no diaphragmatic muscle was present; a small ridge of muscle existed anteromedially. (A very thin hernia sac functioned as an elevated diaphragm, keeping the abdominal contents separate from the chest.) The kidney was removed with an Endobag™ through a 1 cm port site. A deliberate search for a renal artery aneurysm was not performed. Intraoperatively, the surgeons considered whether to place a synthetic patch in place of the missing diaphragm. Noting her normal pulmonary function tests, they elected to defer action on the diaphragm until a later time.

Both anti-hypertensives were held on the evening prior to surgery. In the immediate post-operative period, pain was reduced with morphine, but she reported tenderness at the laparoscopy sites. Four hours post-operatively, resting blood pressures were 125/75, and she received 0.25 mg/kg amlodipine. She vomited 20 min after the dose, but pressures improved to 102/52. At discharge (18 h later), this dose was continued once daily. The drug was weaned and discontinued within 3 weeks.
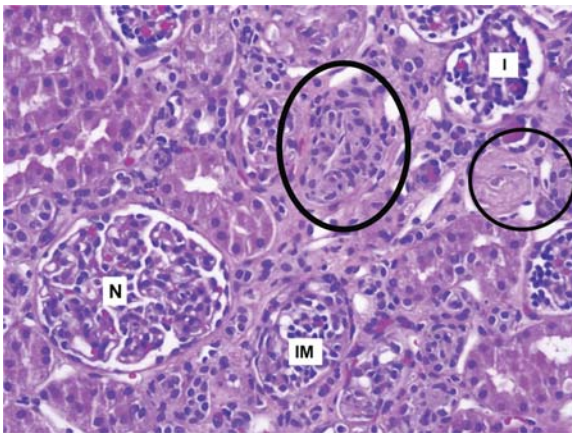
Pathology revealed a hypoplastic immature kidney measuring 5 × 3 × 2 cm and weighing 15 g (expected weight for age ~60 g). The collecting system and medullary pyramids showed no evidence of obstructive uropathy. The renal cortex showed hypoplasia with some glomerular immaturity and moderate glomerulosclerosis

Fig. 1. Nuclear renal scan.

Fig. 2. Time-resolved, dynamic contrast-enhanced MRA of the chest and abdomen.

Fig. 4. A cross-section view of the distal renal artery which shows medial hypertrophy and florid peri-arterial 'fibroid-like' smooth muscle nodules (HE ×40).

Fig. 5. Bundles of smooth muscle cells streaming from the artery wall (A) to form peri-arterial fibroid-like nodule (N). Focal lymphocytes and fibrous tissue were also noted (open star) (HE ×100).

Fig. 6. Light microscopy of the renal cortex showing medial arteriolar hypertrophy with luminal narrowing (oval). Glomeruli vary from normal (N) to sclerosed (circle), while others show immaturity with persistent epithelial cell prominence (IM) (HE ×200).

and patchy tubulo-interstitial atrophy (Figure 4). The main renal artery was small and the wall showed moderate medial hypertrophy. Also noticed was the presence of

prominent smooth muscle nodules surrounding the artery and some of its main branches (Figures 4–6). Although blood pressures in our patient were modestly elevated, such changes can be found within end-stage kidneys and are attributed to severe hypertensive damage to arteriolar walls. Smooth muscle regeneration forms 'fibroid-like' nodules. This suggests the presence of intermittent unkinking of the proximal artery with high pressures reaching the distal renal artery. The renal cortex showed hypoplasia with some glomerular immaturity and moderate sclerosis and patchy tubulo-interstitial atrophy (Figure 6). Intrarenal arteries and arterioles displayed moderate luminal narrowing due to medial hypertrophy; however, fibrinoid necrosis, onion-skinned arterioles and juxtaglomerular apparatus abnormalities were absent.

Discussion

This patient's ultrasound did not reveal a small, scarred or dysmorphic kidney to suggest an explanation for the hypertension. Analyzing this case prospectively, hypertension might occur if renin secretion from a solitary kidney was elevated. Captopril-augmented renal scanning or angiography can assess for vascular abnormalities [7], but the sensitivity of captopril scans has been criticized [8]. Angiography is invasive. Here, the left kidney's large size was thought to indicate compensatory growth, suggesting that the right kidney had been abnormal or absent for most or all of her life. This led to the decision to search for renal tissue elsewhere. Since an ectopic kidney might not appear reniform nor be of normal size, a functional nuclear medicine study was performed. After the location was known, MRI was used to provide anatomic detail. Valentini *et al.* [3] described hypertension attributed to a unilateral, malformed kidney. In that case, the defect was detected by MRI when control of pressures proved to be suboptimal after 1 year of pharmacologic therapy. Ilyas and Tolaymat [2] described a patient in whom only retrograde pyelography enabled the detection of the abnormal kidney. In our patient, an initial renal ultrasound failed to detect the right kidney, and therefore, looking for an abnormal kidney within the physiologic location would not have succeeded. In this case, the abnormal kidney had sufficient function to enable detection by nuclear imaging, evident from her peripheral renin activity and aldosterone levels.

Scintigraphic uptake in the right chest was amorphous, making it impossible to define the limits of the organ or to measure differential function. In addition, there was interference from nearby blood pool activity. In this case, nuclear imaging attracted attention to an unlikely place in which a missing kidney could be found. Though angiography is the gold standard for defining renal arteries and collateral vessels, it is infrequently used in pediatrics due to its invasiveness. MRA has become more useful as it becomes possible to visualize smaller vessels. In children, MRA usually requires sedation. CT angiography permits more rapid image acquisition, sometimes enabling studies without sedation, but with significant radiation exposure. Prior to 2007, it was not possible to obtain the dynamic, contrast-enhanced time-resolved angiography used in this case.

Prenatal ultrasounds did not prospectively detect the diaphragmatic eventration, ectopic renal position nor the abnormal renal size. These were reviewed after the diagnosis was known, and in retrospect, although both kidneys appeared in the normal position, the right hemidiaphragm was not definitively identified.

The virtual absence of a right hemidiaphragm was not known until laparoscopy. Preoperative MRI images of the ectopic kidney were suggestive of a Bochdalek hernia, demonstrating the bowel and the kidney within the thorax. Standard X-rays suggested the presence of an eventration of the hemidiaphragm. The complete hernia sac mimicked an eventration, or high-riding diaphragm on X-ray and intraoperatively. The patient's pulmonologist elected not to recommend diaphragmatic reconstruction.

When the small, ectopic kidney was found, physicians discussed nephrectomy with the family. It was hoped that the kidney might involute without the need for surgery. Normalization of the pressure, however, was a priority, especially in light of mild left ventricular hypertrophy on echocardiography. The first agent offered was an angiotensin-converting enzyme inhibitor (ACEI). Bilateral renovascular hypertension is a contraindication to the use of an ACEI. Some consider suspicion of renovascular hypertension as a general contraindication, even when unilateral [1]. A non-invasive, pharmacological destruction of the affected kidney was desired in this case, and suspicion of disease in the contralateral kidney was low.

Despite drug-related fatigue attributable to the ACEI, the family still hoped to find a tolerable pharmacologic strategy. An angiotensin receptor blocker and a calcium channel blocker reduced pressures without adverse effects, but not below the 90th percentile. After nephrectomy, pressures improved, but did not immediately normalize. Pain in the post-operative period might have elevated her pressures, though her examination suggested that pain was well controlled. Having anticipated continued post-operative hypertension, we did not assess the cause. Levels of renin and aldosterone are not interpretable while receiving antihypertensives, and the pressures remained normal as doses were weaned. Hypotension did not occur.

Laparoscopic nephrectomy is a relatively new option, with less morbidity than open nephrectomy. Gupta *et al.* compared 505 retroperitonoscopic approaches to 115 open procedures in adults. Blood loss and post-operative length of stay were much lower with endoscopy. Six per cent of the endoscopic attempts had to convert to an open case. Operative time averaged 85 min with endoscopy and 70 min for open nephrectomy [9]. Removal of a unilateral poorly functioning kidney eliminates the need for medications in 75% of children and reduces the number of drugs required in almost all [10, 11]. Among those who benefit, hypertension can continue for a few months, but the median time to normalization is 1 week [10]. Even if, before surgery, the abnormal kidney provides more than 13% of total function, blood pressure and glomerular filtration remain excellent 5–16 years after removal [12].

Thoracic renal ectopia is the rarest form of developmental renal anomaly. Few cases of such ectopic kidneys have been occasionally reported previously, but not with peri-arterial smooth muscle nodules. This pathology has been described in arterioles of end-stage renal disease with marked hypertension. Though this child's blood pressures were higher than the 95th percentile for her age, they were much lower than the pressures typically associated with threats to vessel integrity. We also found none of the pathologic changes to be associated with the obstruction of urine flow.

Many reports of renovascular hypertension in children describe the restoration of renal blood flow using endovascular or percutaneous transluminal angioplasty. Others describe nephrectomy when the normalization of flow is not possible. Tilemis *et al.* [13] compared nephrectomy with pharmacologic treatment in a unilateral multicystic dysplastic kidney (MCDK), where spontaneous involution is almost universal. Comparing 21 children who underwent nephrectomy with 20 who did not, outcomes were identical within 6 years. But when the malformation is not MCDK, discrete arterial stenosis or part of a recognized syndrome, we have little information with which to predict the natural course. Well-known limitations of pharmacologic management include non-adherence, medication side effects and medication failure. Although 'pharmacologic nephrectomy' is an attractive idea to parents and caregivers, after the review of the literature, we conclude that new techniques make nephrectomy the preferable solution for hypertension in the context of a malformed, poorly functioning kidney.

References

1. Tullus K, Brennan E, Hamilton G *et al.* Renovascular hypertension in children. *Lancet* 2008; 371: 1453–1463
2. Ilyas M, Tolaymat A. Hypertension and the vanishing kidney. *Pediatr Nephrol* 2005; 20: 229–231
3. Valentini RP, Langenburg S, Imam A *et al.* MRI detection of atrophic kidney in a hypertensive child with a single kidney. *Pediatr Nephrol* 2005; 20: 1192–1194
4. Hahn H, Park SY, Eom JH, Park SW. Quiz page. Congenital intrathoracic kidney after regression of an adrenal mass. *Am J Kid Dis* 2009; 53: A27–A28
5. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004; 114: 555–576
6. Han BK, Babcock DS. Sonographic measurements and appearance of normal kidneys in children. *Am J Roentgenol* 1985; 145: 611–616
7. Lagomarsino E, Orellana P, Munoz J *et al.* Captopril scintigraphy in the study of arterial hypertension in pediatrics. *Pediatr Nephrol* 2004; 19: 66–70
8. Lenz T, Kia T, Rupprecht G *et al.* Captopril test: time over? *J Hum Hypertens* 1999; 13: 431–435
9. Gupta NP, Hemal AK, Mishra S *et al.* Outcome of retroperitoneoscopic nephrectomy for benign nonfunctioning kidney: a single-center experience. *J Endourol* 2008; 22: 693–698
10. Johal NS, Kraklau D, Cuckow PM. The role of unilateral nephrectomy in the treatment of nephrogenic hypertension in children. *BJU Int* 2005; 95: 140–142
11. Baez-Trinidad LG, Lendvay TS, Broecker BH *et al.* Efficacy of nephrectomy for the treatment of nephrogenic hypertension in a pediatric population. *J Urol* 2003; 170: 1655–1657
12. Hegde S, Coulthard MG. Follow-up of early unilateral nephrectomy for hypertension. *Arch Dis Child Fetal Neonatal Ed* 2007; 92: F305–F306
13. Tilemis S, Savanelli A, Baltogiannis D *et al.* Is the risk of hypertension an indication for prophylactic nephrectomy in patients with unilateral multicystic dysplastic kidney? *Scand J Urol Nephrol* 2003; 37: 429–432