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Evaluation and management of bilateral renal artery stenosis in children: a case series and review

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Abstract. This report describes the clinical course, diagnostic evaluation and management of six children with bilateral renal artery stenosis (RAS) and concurrent narrowing of the abdominal aorta. Except for one child with active arteritis, the others were asymptomatic. There were no clinical or laboratory features suggesting the etiology of hypertension in four of six patients, and diagnostic procedures, including Doppler duplex ultrasound and captopril scintigraphy, were unreliable in screening for such hypertension. Abdominal aortography and selective renal angiography confirmed the diagnosis of bilateral RAS and associated anatomical alterations of the aorta and its branches. The hypertension was severe and minimally responsive to antihypertensive agents. It was cured or improved after percutaneous transluminal angioplasty (PTA) of three vessels in two children with mid-vessel stenoses, while hypertension persisted after PTA of two mid-vessel stenoses in a third child and one vessel with ostium stenosis in a fourth child. Autotransplantation of seven kidneys in four children resulted in cure or significant improvement of the hypertension. Renal function was preserved in all children during a mean follow-up time of 41 months. Based on illustrative data from these six children, as well as information from a review of the literature, this report discusses the key diagnostic issues and stresses the potential advantages of renal autotransplantation in selected children with this disorder.

Key words: Hypertension – Renal artery stenosis

Introduction

The diagnosis and management of bilateral renal artery stenosis (RAS), often accompanied by narrowing of the abdominal aorta, or, mid-aorta syndrome, is very challenging. Antihypertensive agents are either ineffective in controlling such hypertension or have the potential risk for acute renal ischemia. Moreover, life-long need for medications may be associated with noncompliance, high cost and adverse effects. The utility and effectiveness of percutaneous transluminal angioplasty (PTA) may also be limited due to the frequent occurrence of stenosis involving the ostium and concurrent aortic disease. In such children decisive treatment is essential to preserve glomerular filtration rate (GFR) and to limit vital organ injury due to systemic hypertension. The current case series and a review of the pediatric literature provide a basis for the diagnosis and management of this disorder.

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Current case series

Pertinent clinical, laboratory and radiological features of six children with severe and intractable hypertension (>99th percentile for age) [1] due to bilateral RAS as well as severe abdominal aortoocclusive disease or "middle aorta syndrome" are shown in Table 1. Patient 2 was the only one with symptoms attributable to hypertension. This child and patient 6 were the only two with clinical signs which led us to suspect RAS. In all six children, urinary findings were either absent, minimal or nonspecific and renal function was intact. A standardized oral captopril test [2] was performed in patients 1 and 6 prior to starting antihypertensive medications and a sixfold rise in post-captopril plasma renin activity occurred in patient 1. Unstimulated peripheral renin activity was increased by two- to ten-fold above normal limits for age [3] in all children, but these results often became available after the angiographic diagnosis of RAS and, therefore, were not utilized in deciding the type of revascularization to be performed. Also, renal vein levels were measured in three patients and, although suggestive of bilateral RAS, the results did not alter the treatment plan based on arteriography alone. A ^{99m}technetium-diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) scan was performed before and after oral captopril

Table 1. Selected clinical, laboratory and radiological studies in six children with bilateral renal artery stenosis (RAS) and abdominal aortoocclusive disease

Patient no.	Age, race, sex diagnosis	Presenting symptoms and signs	Laboratory-studies	^{99m}Tc-DTPA scan	Renal-ultrasound	Arteriography	Intervention	BP results (mmHg)[a] creatinine (mg/dl) follow-up
1	11 years WF No specific diagnosis	Asymptomatic; BP 215/150 on pre-operative examination for adenoidectomy; grade II retinopathy; periumbilical bruits	1+ proteinuria; serum creatinine 0.5 mg/dl. Positive oral captopril test	Decreased flow to RK; split function 57% LK, 43% RK	Normal kidneys and vessels, narrowed mid-abdominal aorta	90% mid-vessel stenosis in L renal artery, 75% stenosis in branch to R lower pole, extensive narrowing of SMA and aorta, many renal collaterals	Bilateral PTA on two occasions; multiple PTA of aorta	Improved (120/85) 0.8 3.9 years
2	2.8 years WM Takayasu's arteritis	Fever, anorexia, conjunctivitis, weight loss, S_3 gallop, pulmonary edema, seizures, BP 160/120, periumbilical bruits	1–2+ proteinuria (0.2 g/day), serum creatinine 0.4 mg/dl, potassium 2.8 mmol/l	Decreased flow; split function 96% LK, 4% RK. DMSA scan: no function RK	Normal 10 weeks earlier; constricted abdominal aorta on repeat study, LK 8.1 cm, RK 5.6 cm	Severe L ostium RAS, narrowing of abdominal aorta (3.2 mm). No visualization of the RK	R nephrectomy L splenorenal anastomosis L PTA	Failed Failed Improved (120/75) 0.7 1.3 years
3	3.5 years WM Fibromuscular dysplasia	Asymptomatic; BP 200/120	Serum creatinine 0.3. Peripheral renin level ≥ tenfold of upper normal limit	Decreased flow to RK lower pole; split function 55% LK, 45% RK	Normal kidneys and vessels	90% ostium RAS bilaterally with many collateral vessels; mild smooth narrowing of abdominal aorta	Bilateral ATX	Improved (120/70) 0.4 0.5 years
4	4 years WF Fibromuscular dysplasia	Asymptomatic; BP 180/110 on evaluation for heart murmur	Serum creatinine 0.4 mg/dl. Renal vein renin studies: lateralize to LK	Equal split function	Normal renal size and vessels, narrowed abdominal aorta	90% mid-vessel stenosis bilaterally, narrowed abdominal aorta	Bilateral PTA Bilateral ATX	Failed Improved (120/70) 0.5 3.1 years
5	13.9 years WM Fibromuscular dysplasia	Asymptomatic; BP 210/160 on examination after finger fracture; L periumbilical bruit	Serum creatinine 0.7 mg/dl. Renal vein renin studies: lateralize to LK	Split function 40% RK, 60% LK	Normal	Poor visualization of RK, 90% ostium RAS bilaterally with many collateral vessels; narrowed abdominal aorta, occluded SMA	Dacron bypass of aorta and renal arteries Thrombosed R graft. R ATX	Failed Improved after R ATX, (130/70) 1.0 10.8 years
6	5.2 years WM Neurofibromatosis	Asymptomatic; BP 180/100 on routine examination; café au lait spots and Liesh nodule L iris; periumbilical bruits	Serum creatinine 0.4 mg/dl. Negative oral captopril test. Renal vein renin studies: no lateralization	Split function 78% RK, 22% LK	Normal renal size and narrowed R abdominal aorta	90% ostium RAS bilaterally; severe stenosis of abdominal aorta and iliac axis, stenosed R iliac artery	R PTA Goretex graft bypass of aortal bilateral ATX	Failed Cured 0.6 3.9 years

PTA, Percutaneous transluminal angioplasty; ATX, autotransplantation; SMA, superior mesenteric artery; ^{99m}Tc-DTPA, ^{99m}technetium-diethylenetriamine pentaacetic acid; W, white, F, female; M, male; BP, blood pressure; LK, left kidney; RK, right kidney; DMSA, dimercaptosuccinic acid

[a] "Cure" is defined as normalization of BP to below 95% for age without antihypertensive medications; "improvement" is defined as a decrease in diastolic BP by ≥15 mmHg with concurrent non-angiotensin converting enzyme inhibitor (ACEI) antihypertensive medications [1]; "failed" is defined as the need of ACBI to control BP or failure to reduce the diastolic BP by ≥15 mmHg after a revascularization procedure

administration in all but patient 5, and bore little relationship to the angiographic findings, especially in patients 3, 4 and 6. Duplex Doppler ultrasonography failed to identify RAS, despite clinical signs and symptoms suggesting this disorder in patients 2 and 6.

All children underwent abdominal aortography in the frontal position and selective renal artery injections of contrast with oblique views. Except for patient 2 who had cut-film angiography, all others had digital angiography. The treatment plans were highly individualized because the

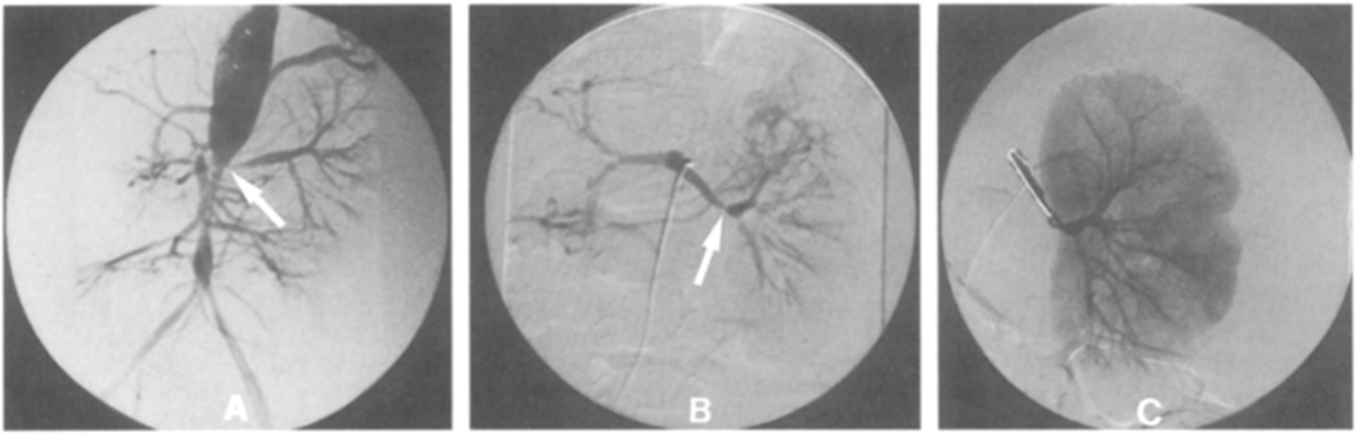

Fig. 1. Selective renal angiograms of patient 2. **A** Ostium stenosis of the left renal artery (*arrow*), nonvisualization of the right renal artery and marked narrowing of the abdominal aorta are evident. **B** Repeat study after right nephrectomy and left splenorenal anastomosis demonstrating a marked stenosis (*arrow*) at the clamp site distal to the surgical vascular anastomosis. **C** Improved blood flow is evident following percutaneous transluminal angioplasty with subsequent improved control of hypertension

Table 2. Causes and revascularization procedures for bilateral RAS in 52 children managed over the past decade

Reference	*n*	Age, sex, diagnosis, follow-up time	Procedures	Results of follow-up[a]
Current series	6	(see Table 1)	1 PTA	Improved
			1 R nephrectomy and L splenorenal bypass	Improved
			3 Bilateral ATX	Improved
			1 Unilateral ATX	Cured
Milner et al. [4]	1	9 years, F, Takayasu's arteritis, 12 months	Bilateral Goretex arterial bypass	Thrombosis at 12 months, anuria, death
	1	8 years, F, Takayasu's arteritis, 18 months	Bilateral Goretex arterial bypass	Thrombosis, anuria at 18 months
			Unilateral ATX	Cured
	1	4 years, F, Takayasu's arteritis, 3 months	Bilateral ATX	Failed
	1	8 years, M, Takayasu's arteritis, 36 months	None	Normal BP, cardiomyopathy
Alon et al. [5]	1	12 years, M, fibromuscular dysplasia, 24 months	PTA	Failed
			R hypogastric bypass; occluded, restenosis	Failed
			L ATX	Hypertensive
			R restenosis repair	Cured
Merguerian et al. [6]	1	16 years, M, abdominal aortic hypoplasia, 48 months	Bilateral ATX	Cured
	1	12 years, F, Takayasu's arteritis, 17 months	Bilateral ATX	Cured
	1	12 years, F, no diagnosis available, 14 months	R PTA	Thrombosed
			R ATX	Failed
			R nephrectomy	Failed
			L ATX	Cured
Berkowitz and O'Neill [7][b]	6	Mean age 10.3 years, mean follow-up to 55 months	R and L aororenal saphenous vein bypass; 2/6 Dacron-reinforced	4 Cured 2 Improved
	6	Mean age 9.2 years; mean follow-up 51 months	Aorto-aortic Dacron bypass R and L saphenous vein bypass; 4/6 Dacron-reinforced	5 Cured 1 Improved
Lacombe [8] and personal communication	14	Mean age 11.2 years, mean follow-up 102 months	8 ATX (1 bilateral) 1 of 6 Nephrectomy 1 of 6 Revascularization 7 Revascularization	12 Cured 2 Improved
Eke et al. [9]	1	11 months, M, Takayasu's arteritis, 54 months	R PTA	Failed
			R ATX	Hypertensive
			L ATX	Improved
	1	14 years, M, Takayasu's arteritis, 20 months	R ATX	Hypertensive
			L PTA	Failed

[a] "Failed" after ATX or bypass graft means revascularization failure as opposed to "hypertensive" which means vascular success; "cured" means normal BP for age and sex without use of medications while "improved" indicates continued use of medications

[b] Sex and diagnosis were not specified; in this series most children had nonspecific arteriopathy or fibromuscular dysplasia

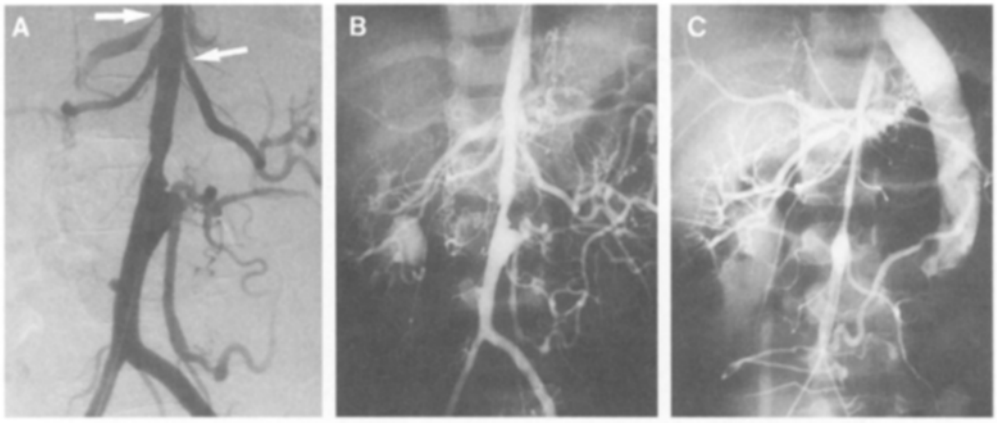

Fig. 2. Renal angiograms of patient 5 with neurofibromatosis. **A** Severe bilateral renal artery ostium stenosis is evident (*arrows*); note unusual high takeoff of right renal artery, atypical coarctation of the infrarenal aorta and larger caliber of the left iliac artery. **B** Later angiographic frame showing filling of the right collecting system with delayed visualization of the left kidney, occlusion of the superior mesenteric artery with most of the splanchnic circulation supplied by the inferior mesenteric artery and numerous collateral vessels to the kidneys and mesenteric bed. **C** Oblique aortogram showing generous Dacron prosthetic graft bypassing the aortic narrowing and left renal autotransplantation with contrast material being faintly visible in the left iliac fossa. Two months later the right kidney was autotransplanted and the ciliac arterial stenosis was bypassed resulting in normotension and resolution of abdominal angina symptoms

severity, location and segment length affected by stenosis as well as the etiology and extent of aortooclusive disease were highly variable among patients. In patient 1, extensive mid-renal arterial stenosis and aortic narrowing precluded surgical repair. Hypertension in this patient was satisfactorily managed with successive PTA of all the involved vessels.

Patient 2, with Takayasu's arteritis, was managed with corticosteroids which together with bilateral RAS contributed to the development of medically intractable hypertension. The evolving arterial changes are shown in Fig. 1. Treatment with sublingual nifedipine and intravenous labetalol was ineffective. A brief course of captopril resulted in mild deterioration in renal function and only transient improvement in systemic blood pressure. Intravenous labetalol and oral veraparamil at high dosages were also ineffective. Accelerated hypertension, congestive heart failure and seizures occurred 3 days after institution of furosemide. In this child one kidney with marked renal dysfunction was removed and a splenorenal arterial anastomosis followed by PTA at the site of vascular clamp-induced stenosis improved the hypertension.

Patients 3, 4 and 5 had the intimal form of fibromuscular dysplasia. Patient 3 had ostium stenosis involving all three renal arteries with minimal abdominal aortic narrowing. Because of the severity of his hypertension, he was begun on sublingual nifedipine and intravenous labetelol with minimal effect. The addition of intravenous sodium nitroprusside was equally ineffective in reducing systemic blood pressure. Because the interventional radiologist felt that the severity and location of RAS precluded PTA, both kidneys were autotransplanted in a single operation with anastomosis to the common iliac vessels. Patient 4 failed to respond to sublingual nifedipine as well as to intravenous labetelol and sodium nitroprusside. Moreover bilateral PTA of the mid-vessel stenosis did not relieve the hypertension, whereas blood pressure improved after staged Goretex bypass of the aorta and unilateral renal autotransplantation followed by autotransplantation of the remaining kidney 2 months later. Patient 5 had minimal response to intravenous sodium nitroprusside. He was then managed with a Dacron graft to bypass the aorta, superior mesenteric artery and both renal arteries. However, blood pressure remained high after surgery due to a thrombosis of the bypass graft to the right kidney. This kidney was successfully autotransplanted in the right iliac fossa and hypertension subsequently improved markedly.

Patient 6 had neurofibromatosis and severe hypertension. Sublingual nifedipine was ineffective. Angiography revealed severe aortic, renal ostium and extrarenal vascular obstruction. PTA of the right renal artery was unsuccessful in dilating this vessel. The hypertension was cured after Goretex bypass of the aorta and staged bilateral renal autotransplantation, as in patient 4. In both of these patients aortoaortic bypass grafts were utilized to improve distal aortic blood flow and to accomodate eventual linear growth.

During follow-up ranging from 0.5 to 10.8 years (41.5 ± 33.5 months), five patients had well-controlled blood pressure on minimal dosages of monotherapy (calcium channel inhibitor) and one child was cured. All patients have maintained excellent renal function during this follow-up period with serum creatinine concentrations ranging from 0.4 to 0.9 mg/dl and creatinine clearances ranging from 95 to 132 ml/min per 1.73 m^2.

Discussion

In addition to our six cases, Table 2 summarizes the data from 36 children reported over the last decade in which it is possible to determine treatment and outcome of bilateral RAS [4–9]. Not included in Table 2 are data from three large series which included another 64 children with bilateral RAS in whom such information is not available [10–12]. Unfortunately, many of these reports do not

provide details relating to the diagnosis of this disorder. However, all of these studies emphasize the relative ineffectiveness of medications while underscoring the merits of revascularization to control hypertension and to preserve renal function in these children.

Diagnosis of RAS

At the present time there are no reliable noninvasive screening methods for RAS and there are no imaging techniques that may exclude children who need not undergo angiography. In adults, the diagnosis of RAS is often suggested by Duplex renal ultrasonography [13–15], but the effectiveness of this modality is reduced in bilateral RAS and in branch disease, as well as with the intimal form of fibromuscular dysplasia which is a more common cause of RAS in children than in adults [11, 16–18]. This modality failed to detect RAS in five of our six patients who subsequently were shown to have angiographically and clinically important bilateral RAS.

Radionuclide scintigraphy performed before and after angiotensin converting enzyme inhibitors (ACEI) has been used extensively to help predict the presence of RAS using the differential functional response of renal blood flow and GFR to ACEI [19–24]. A reduction in effective renal plasma flow or GFR of more than 40% in response to captopril during ^{131}iodine(I)-orthohippurate, ^{131}I-hippurate, ^{99m}Tc-DTPA or ^{99m}Tc-dimercaptosuccinic acid (DMSA) scintigraphy may be helpful in identifying patients with "critical RAS" in whom pharmacological management should be avoided. However, the lack of validity data with these scintigraphic methods in children, and a precision rate under 50% in predicting a good response to revascularization in unselected adults with refractory or severe hypertension due to bilateral RAS [22], limits the overall utility of these screening methods. The captopril ^{99m}Tc-DPTA scan was suggestive of renovascular hypertension in only two of our six patients. However, in one of these two children (no. 2) renal scintigraphy showed only a 4% contribution to total renal function from the right kidney and nonvisualization of this kidney by arteriography led to a nephrectomy; the pathological findings demonstrated healthy renal tissue. In retrospect, a frozen section biopsy of this kidney at the time of surgery may have led to an attempt at autotransplantation. Newer methods for detecting RAS include ^{99m}Tc-metcaptoacetyltriglycine scanning and magnetic resonance angiography [25, 26]. However, neither of these examinations were performed in a pediatric population.

The oral captopril challenge test and its modifications have been useful in predicting angiographically confirmed RAS in adults [2, 27]. This test has a high sensitivity, moderate specificity and is particularly useful when it is negative, since it effectively excludes RAS; however, the positive predictive value (percentage of patients with a positive test and significant RAS) is about 35%, even when performed in a population with a high prevalence of renovascular hypertension [28]. Drawbacks of published studies include performance of the captopril test in highly selected patients, dissimilar protocols used to perform the test, reliance on one or more measurements of plasma renin activity, different degrees of RAS used to define the disorder angiographically or by blood pressure response after revascularization and absence of validity data in children. One study in hypertensive children who were selected by having a normal urinalysis and GFR together with a non-diagnostic renal ultrasound or intravenous urogram, found that only three of seven children (43%) with a positive captopril challenge test had arteriographic abnormalities, but that one of two with a negative test also had RAS [29]. This study concluded that the captopril challenge test was inadequate for diagnosing RAS in children and adolescents despite the high prevalence of the disorder in this selected population. Another test which relies on a hypotensive response 2 h after oral captopril (0.7 mg/kg) may be useful in defining hypertension due to high circulating renin states, but its usefulness in screening specifically for RAS has not been well established [30]. In addition to the problems described above, none of these noninvasive studies can reliably distinguish unilateral from bilateral RAS.

Invasive evaluation by selective renal vein renin measurement has proven useful in the screening of children with suspected RAS and for predicting blood pressure response to surgical or nonsurgical revascularization [12, 17, 31, 32]. However, median renal vein renin ratios are lower in children with bilateral RAS than unilateral RAS (1.2:1 vs. 1.5:1) and are therefore less predictive of outcome following revascularization [10]. Collateral vessel formation, as occurred in patients 1, 3 and 5 of the current series, may provide sufficient renal perfusion and tissue viability despite severe main renal artery stenosis. In such instances renin release may be high but unequal from the two kidneys, resulting in misleading lateralization of renin activity.

The foregoing discussion supports our view that an abnormal result in one of several screening tests for RAS may identify hypertensive children who should undergo angiography. However, a "normal" result on such testing cannot be relied on to exclude children with a high index of suspicion for RAS who require angiography. Clinical features suggesting RAS include: pre-adolescent children with severe hypertension (>99th percentile for systolic or diastolic blood pressure) who may be refractory to non-ACEI regimens; fall in blood pressure and/or a decrease in GFR with ACEI; signs of neurofibromatosis, tuberculosis, Williams' syndrome, aortic coarctation or active arteritis; presence of flank or periumbilical bruits; normal renal function studies together with urinary findings not suggestive of renal parenchymal disease; asymmetry in renal size by renal ultrasound or intravenous urography. Since most children with hypertension due to RAS are asymptomatic, our current approach is to postpone medical treatment until appropriate evaluation is performed. In such children we first recommend an oral captopril test (0.7 mg/kg, maximum 25 mg) with blood pressure measurements and with measurement of renin activity before and 1 h after captopril. Random peripheral renin activity and renal vein renin sampling are no longer routinely performed at our center. We also obtain an ACEI-assisted ^{99m}Tc-DTPA scan. If both or either of these studies are normal and suprarenal coarctation of the aorta is excluded, arteriography is postponed until results are available from biochemical studies

used to exclude the presence of hyperthyroidism, hyperaldosteronism, pheochromocytoma or other neuroendocrine tumors. This is followed by abdominal aortography in the frontal projection and selective renal angiography in the appropriate oblique positions. The latter is very important in investigating the presence of intrarenal arterial disease, which may influence the choice of pharmacological agents or revascularization procedure needed in the individual patient. We routinely employ intraarterial digital subtraction angiography (IADSA) [33] for diagnosis and anatomical definition of RAS. IADSA is performed after intravenous sedation to limit motion. This technique is faster than conventional cut-film angiography and is ideal for monitoring renal artery angiography or other vascular interventions.

Management of bilateral RAS

Medical management. As in other reports, pharmacological management in five of our six patients was quite disappointing [6, 7, 9, 16, 34, 35]. This refractoriness to medical management can be largely explained on the basis of the one-kidney, one-clip Goldblatt model of hypertension which best resembles the clinical aspects of bilateral RAS [36, 37]. In this model, renal hypoperfusion leads to circulatory volume expansion via renin release and angiotensin II-induced stimulation of aldosterone and, perhaps, vasopressin; unlike unilateral RAS, however, there is no modulation of this process by pressure natriuresis by the unaffected kidney [36–41]. Usual measures of managing hypertension, such as restriction of sodium intake or use of diuretic agents, generally fail to reduce the hypertension because such measures enhance renin release [36]. Younger children may respond to antihypertensive drugs with paradoxical increases in systemic blood pressure, possibly due to a more active renin-angiotensin mechanism than in adults [3]. Similarly, blockade of the renin-angiotensin-aldosterone mechanism may convert the hypertension from a predominantly renin-dependent state to a more volume-dependent state [36]. Oral captopril, enalapril or lisinopril or intravenous enalaprilat are generally effective in reducing systemic blood pressure [42, 43], but may occasionally result in renal ischemia without an appreciable change in serum creatinine levels or GFR [44, 45]. These effects are often exacerbated in patients with RAS bilaterally or with a solitary kidney because they lack a compensatory mechanism for increasing GFR [44, 46].

Reported rates of acute renal failure associated with ACEI are 17% and 23% for bilateral RAS [42, 44], 38% for RAS in a solitary kidney [44] and 6% for unilateral or low-grade RAS and hypertension [43]. The risk of ACEI-induced acute renal failure increases with depletion of circulatory volume by salt restriction, use of diuretic agents and with the severity of the stenosis [44, 46–49]. These factors were probably instrumental in both the renal failure and accelerated hypertension in patient 2 which occurred shortly after the start of the diuretic therapy. If ACEI become necessary, particularly after revascularization, the serum creatinine and kidney size and creatinine clearance should be rechecked in about 72 h and at regular intervals, in order to determine the safety of continuing use of such agents. ^{99m}Tc-DTPA split renal function measurements may also be compared with pre-treatment values in patients with declining renal function after starting ACEI. Long-term use of such agents, albeit effective and well tolerated, may result in deterioration in renal function in experimental RAS [50] and in humans [47, 48, 51], due to chronic ischemic tubular injury and fibrosis.

These pathophysiological considerations led us to utilize agents which are less likely to stimulate renin release. Calcium channel inhibitors may be used because they are generally accompanied by little compensatory renin release and minimal effects on GFR [52]. Labetalol and α-adrenergic blocking agents may suppress compensatory release of renin and may also be useful in moderating the effects of norepinephrine which may contribute to the pathogenesis of renovascular hypertension in animal models [53]. In hypertensive children with suspected RAS, salt intake should be moderate and diuretic use should be avoided. As in patient 2 of the current series, the hypertension of arteritis is particularly resistant to routine medical management. Such disorder may benefit most from the use of corticosteroids since the hypertension may improve spontaneously with resolution of the inflammatory process [10].

Revascularization procedures. PTA or surgical revascularization should be considered in all children with RAS, since these procedures have the potential of eliminating the need for life-long pharmacological therapy while preserving renal function. Poor blood pressure control, intolerance to medical therapy or a reduction in renal function after appropriate pharmacological therapy are, perhaps, less important indications for a revascularization procedure.

Percutaneous transluminal angioplasty. Compared with surgical revascularization, PTA is associated with a lower morbidity, shorter time of hospitalization and lower cost. Hypertensive children with more than 75% stenosis in a renal artery may qualify for PTA, particularly if collateral vessels are present and if screening studies and clinical findings exclude other causes of hypertension. An extensive review of this procedure in adults revealed a 24% rate of cure and a 43% rate of improvement [54]. A review of the more limited pediatric experience found that PTA has a high margin of safety and is particularly effective in fibromuscular dysplasia [9 of 10 procedures cured or improved hypertension) [35, 55]. Thus, when this disorder is suspected, PTA should be the primary procedure, particularly when the stenosis is beyond the ostium of the renal artery. A skilled interventional radiologist equipped with microballoons may gain access to and dilate or selectively embolize vessels with an internal diameter as small as 1 mm. In contrast, ostium lesions, syndromes with aorto-renal involvement such as neurofibromatosis, Williams' syndrome or mid-aortic disease with bilateral RAS, as in the current cases, have a poorer outcome and a higher complication rate with PTA than with surgical correction [55–60]. In such instances surgery may be favored from the onset, as was the case in patients 3 and 5 of the current series. It should be noted that the overall experience with PTA is limited in children with bilateral RAS (Table 2).

Table 3. Guidelines for selection of children with RAS for renal autotransplantation[a]

1.	Children under 2 years of age, in whom in situ revascularization is technically difficult
2.	Stenosis of distal renal artery or its hilar branches in which extracorporeal reconstruction is considered
3.	Stenosis in multiple renal arteries
4.	Aneurysm formation plus stenosis
5.	Abdominal aortic hypoplasia or middle abdominal aorta syndrome sparing the iliac vessels
6.	Severe RAS in solitary kidneys
7.	Progressive renal impairment despite medical control of BP after PTA and/or bypass techniques with saphenous vein or arterial autografts
8.	Severe RAS refractory to PTA in whom renal ischemia becomes evident after ACEI or by evaluation with ^{99m}Tc-DTPA captopril scintigraphy

[a] Simultaneous bypass of coexisting severe coarctation may be needed

This procedure controlled hypertension in only one of three patients who received PTA alone and failed in four additional patients when used as an adjunct to surgery. In selected patients in whom PTA of a smaller (< 1 mm) segmental arterial stenosis is not possible or a severely atrophic kidney is the source of excessive renin release, transcatheter embolization may be curative and may obviate the need for partial nephrectomy to control hypertension [61].

Surgical revascularization. This takes two major forms: (1) angioplastic reconstruction to bypass the stenosis with synthetic or autologous grafts or, in the case of short lesions, excision and direct aortorenal anastomosis; (2) autotransplantation of one or both kidneys. Simultaneous bypass of the diseased aorta is feasible, carries a relatively low operative risk and should be considered in children with a narrowed abdominal aorta at or above the takeoff of the renal arteries [7, 8, 62–65]. Nephrectomy is an alternative to revascularization if one kidney is both markedly smaller than age-appropriate ultrasonographic standards [66] and contributes less than 10% of renal function.

Several pediatric series demonstrate rates of cured or improved hypertension and preserved GFR surpassing 90% following surgical revascularization performed for unilateral complicated RAS [7, 8, 16, 18, 56]. There are no comprehensive reviews, however, which directly address the complex issues of bilateral RAS. In a 1981 review of 27 hypertensive children with bilateral RAS, 13 underwent nephrectomy in an attempt to control hypertension; excluding 1 patient with bilateral nephrectomy, only 1 of the other 13 patients had cure or improvement of their hypertension [18]. In this series splenorenal arterial bypass grafts or anastomosis was associated with cure or improvement of hypertension in 9 of 14 children (64%) and failure in 5 (36%). Saphenous vein or renal vein bypass of RAS gave similar results. Only 3 of 54 kidneys were autotransplanted, 2 successfully. Overall, hypertension was cured in 11 of 26 children (42%) and improved in 7 others (27%). Abdominal aortic disease requiring simultaneous surgical repair was not a prominent feature of the children in that review [18]. Thus, the results of reconstructive surgery might have been worse had such patients been included, since there is a strong association of aortooclusive disease (20%–50%) and bilateral RAS ([4, 6–9, 12, 67, 68]; present series).

Over the past decade, children with complex bilateral RAS and, often, abdominal aortic disease have had a very favorable prognosis with surgical revascularization and limited use of nephrectomy. In the combined seven series, comprising 52 children with bilateral RAS (Table 2), 36.5% had mid-aortic syndrome. One child managed by PTA alone and one managed with surgery followed by PTA had improved hypertension and preserved renal function; a third child was not treated with any modality; 48 of the 49 remaining children were managed by surgical revascularization. At follow-up (47.0 ± 43.5 months, mean ± SD) hypertension was cured in 73% (36 of 49) and improved in 22% (11 of 49); 48 of 49 had preserved renal function. Only 3 nephrectomies were performed in this more modern series of patients. It should be noted that the long-term benefit of any revascularization procedure requires longitudinal assessment, since the follow-up time in most studies is relatively short. Restenosis may occur due to somatic growth, progression of the underlying etiology of RAS or as a complication of the surgical anastomosis.

Compared with the previous decade, a greater proportion of surgically revascularized patients now undergo autotransplantation after extracorporeal ostial or branch repairs ([6, 8, 11]; current series; Lacombe M, personal communication, 1993). The overall experience in children with bilateral RAS undergoing autotransplantation is detailed in Table 2. Although the proportion of the 11 children with bilateral RAS undergoing autotransplantation in the study of Martinez et al. [11] is not specified, it appears to be large and the overall rate of cured or improved hypertension in the 28 patients under 22 years of age was 96%. Excluding these 11 patients, 19 children, ranging in age from 0.9 to 16 years, underwent renal autotransplantation. The major disorders leading to autotransplantation included fibromuscular dysplasia and Takayasu's arteritis. Of 29 kidneys autotransplanted with a follow-up time of 37 ± 11 months (mean ± SEM), 1 of 2 grafts in 1 child thrombosed leading to nephrectomy, while all others maintained good renal function. Moreover, hypertension was cured or improved in 18 of 20 (89%) patients. The ultimate prognosis in Takayasu's arteritis and bilateral RAS may be the worst with any form of revascularization due to late thrombosis of Goretex arterial grafts (2 of 2 patients) or failure of autotransplantation (1 of 2 patients) occurring in a series of 4 children with this disorder (Table 2 [4]). Long-term follow-up with repeat renal angiography after renal autotransplantation in adults has shown this to be superior to bypass surgery for the treatment of renovascular hypertension [69]. Such studies are not yet available in children.

Autotransplantation has several potential advantages despite the risks, which include temporary nephrectomy and hypothermic perfusion with Ringer's lactate, University of Wisconsin or Euro Collins preservation solutions. In these selected children with extensive renal artery disease, removal, cooling and protection of the kidneys from

ischemic injury permits careful ex vivo microvascular repair with maximal exposure. The proximal aortic disease may be bypassed by connecting the renal artery to the internal iliac vessels, as done in patients 3–6 in the current series. The iliac and hypogastric vessels have excellent compliance, and when used in situ or as autografts they mature with the growing child, thereby decreasing the risk of restenosis or aneurysm formation which may accompany splenorenal bypasses or use of saphenous vein grafts [7, 8, 11, 58, 70]. A staged approach with Dacron or Goretex bypass of the aorta, if this is needed, together with autotransplantation of the more compromised kidney, followed 2–3 months later with autotransplantation of the second kidney, is the approach currently recommended in our patients with combined atypical abdominal aortic coarctation and stenosis in one or both renal arteries that does not respond to a trial of PTA. Guidelines for selection of hypertensive children with severe RAS for autotransplantation are provided in Table 3. These guidelines are broad and their application may depend in part on the microvascular techniques and expertise available at individual institutions.

In summary, abdominal aortography and renal angiography are the only reliable means for confirming the diagnosis of mid-aortic syndrome and/or RAS in children and for formulating the therapeutic strategy. Because hypertension associated with RAS is often severe and medical therapy may be ineffective or risky, PTA or a more definitive surgical revascularization procedure is recommended to help preserve renal function, to prevent injury to other organs and to obviate or reduce the need for life-long use of antihypertensive medications. Guidelines are provided for selecting children with severe bilateral or complex RAS for autotransplantation. However the long-term benefits of this procedure over more conventional operations may be determined only by prospective longitudinal, clinical and angiographic assessments.

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