Renovascular Hypertension in Children

INTRODUCTION

Compromised blood flow to a portion, one, or both kidneys leads to renovascular hypertension (HT) [1]. Renovascular disease (RVD) is an uncommon, but serious and correctable cause of HT in children. In this paper, I will discuss renovascular disease as a cause of pediatric HT.

PREVALENCE

RVD accounts for 5-10% of all cases of HT in children [2]. It is the third most common cause of HT in children following coarctation of the aorta and parenchymal renal disease.

PATHOPHYSIOLOGY

The chief pathophysiologic mechanism underlying renovascular HT involves the activation of both limbs of the renin-angiotensin-aldosterone system and depends on the presence or absence of a contralateral kidney. Unilateral renal ischemia initiates the hypersecretion of renin, which accelerates the conversion of angiotensin I to angiotensin II and enhances adrenal release of aldosterone. The result is profound angiotensin-mediated vasoconstriction and aldosterone-induced sodium and water retention. In the 2-kidney 1-clip model, where the clinical correlate is unilateral renal artery disease, sodium and water handling via pressure diuresis of the contralateral kidney may be sufficient to prevent a volume component to the HT. In the setting of a solitary kidney (experimentally, the 1-kidney 1-clip model), sodium and water handling is compromised, sodium and water retention ensues, and volume-mediated HT occurs [3].

Data show that 11-60% of cases of RVD are familial with a pattern most consistent with autosomal-dominant inheritance with variable penetrance [4]. The renin-angiotensin system plays a part not only in the regulation of blood pressure (BP) but also in vascular modeling. Renal artery stenosis can arise in Williams-Buren syndrome, associated with elastin gene (ELN) mutations [5] and in Alagille syndrome [6] caused by mutations of JAGGED1 (JAG1), which codes for a ligand for NOTCH receptors.

CAUSES

The causes of renovascular disease are presented in Table I. The most common abnormality is renal artery stenosis, which is bilateral in 53-78% of cases, and occurs in combination with intrarenal disease in 31% of cases [7]. Intrarenal disease alone is found in 44% of cases [7].

CLINICAL PRESENTATION

RVD may be diagnosed incidentally in 26-70% of affected children [8]. All children needing more than one drug to control the HT should be investigated for RVD [9]. Children with renovascular HT should undergo investigation for evidence of end-organ damage, since two-thirds of children will have left ventricular hypertrophy, 60% will have hypertensive retinopathy, and 10% renal dysfunction [10]. Many children may have abnormalities of other blood vessels (aorta, cerebral, intestinal).
HT. Hypokalemia may also suggest renovascular etiology of hyperaldosteronism, increased serum renin activity and/or the presence of elevated plasma rennin level [11].

Trauma, transplanted kidneys, history of a vascular insult (renal artery thrombosis, umbilical vessel catheterization, renal trauma, vasculitis, polyarteritis nodosa, Kawasaki, moyamoya, takayasu, renal transplantation, arterial stenosis or thrombosis, chronic allograft nephropathy), renal transplantation, renovascular arterial hypertension, and hypertension with suspicion for renovascular disease.

Extrinsic compression
- Perirenal hematoma
- Neoplasms
- Wilms', neuroblastoma, lymphoma

TABLE I

CAUSES OF RENOVASCULAR HYPERTENSION IN CHILDREN

<table>
<thead>
<tr>
<th>Intrinsic renal artery disease</th>
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</thead>
<tbody>
<tr>
<td>Fibromuscular dysplasia</td>
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<tr>
<td>Most common (70%)</td>
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<tr>
<td>Intimal fibromuscular dysplasia</td>
</tr>
<tr>
<td>Neurofibromatosis type I, williams-buren syndrome</td>
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<tr>
<td>Neonatal history of umbilical vessel catheterization</td>
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<td>Renal trauma</td>
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<tr>
<td>Vascular</td>
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<tr>
<td>Polyarteritis nodosa, Kawasaki, moyamoya, Takayasu</td>
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<td>Renal transplantation</td>
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</tbody>
</table>

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DIAGNOSIS

Renovascular HT should be suspected if the BP is very high (systolic measurements greater than 200 mmHg and 27-126 mmHg higher than the 95th percentile for age, sex and height), if secondary symptoms of elevated BP are noted (cerebral symptoms, heart failure, facial palsy), if HT is not controlled with two or more antihypertensive drugs, presence of an abdominal bruit, presence of vascular disease (neurofibromatosis, tuberous sclerosis), history of a vascular insult (renal artery thrombosis, umbilical artery catheterization, trauma), transplanted kidneys, or the presence of elevated plasma rennin level [11]. Hyperaldosteronism, increased serum renin activity and hypokalemia may also suggest renovascular etiology of HT.

IMAGING

Non-invasive tests
The role of noninvasive imaging techniques in children with suspected renovascular HT is unclear. Renal ultrasound with Doppler imaging is often the initial imaging modality. Renal scintigraphy with 99m-technetium-dimercaptosuccinic acid (DMSA) or 99m-Tc-mercapto-acetyl-triglycine (MAG3) in conjunction with angiotensin-converting enzyme (ACE) inhibitor is a safe, reliable, and cost effective study in the evaluation of renovascular HT and RAS with an overall sensitivity of around 90% [12]. CT angiography is adequate for most patients with disease of the aorta [13]. Magnetic resonance angiography (MRA) is adequate for assessment of the aorta and main renal arteries, and is becoming a popular alternative to the invasive renal angiogram when possible. Renal angiography remains the standard for evaluation of renal artery disease.

Invasive tests
Renal vein renin sampling is a useful technique in children, especially those with bilateral or segmental renal artery stenosis. It allows localization of the ischemic focus. Despite improvements in imaging technology, catheter-based digital subtraction angiography (DSA) remains the most accurate technique for assessment of suspected RVD in children [14].

TREATMENT

All affected children should be treated early with antihypertensive drugs to prevent renal parenchymal damage. Since HT in these patients is severe, BP reduction should be gradual. Treatment starts with antihypertensive drugs consisting of calcium channel blocker, a ß-blocker or both. ACE inhibitors and angiotensin receptor blockers are generally contraindicated because they reduce glomerular filtration pressure leading to renal failure, which is usually reversible upon discontinuation of the medication [3].

Refractory HT unresponsive to optimal antihypertensive drug therapy is an indication for endovascular or surgical intervention. Most affected children need interventional or surgical treatment. Endovascular treatment with or without stenting will cure more than half of the affected children [8]. Renal angioplasty, renal artery stenting, aortic angioplasty with stenting and ethanol ablation are currently used as endovascular treatment methods [15]. An overall positive outcome of percutaneous transluminal renal angioplasty (PTA) occurs in 55% of children, and 85% improvement in those with disease restricted to one or both renal arteries [16]. The technique is safe, and is the treatment of choice in children who develop malignant HT in spite of aggressive medical treatment.

Surgical procedures including revascularisation and sometimes nephrectomy for a small poorly functioning kidney may also be performed. Cure occurs in 36-70% of patients, and improvement in another 26-56% [10].

When surgery fails, further drug treatment may be carefully tried, including the use of ACE inhibitors and angiotensin receptor blockers, and the direct renin inhibitor, aliskiren. Treatment provided by a multidisciplinary team of pediatric nephrologists, interventional radiologists and vascular surgeons yields excellent long-term results [8, 11].

SUMMARY

RVD accounts for 5-10% of all cases of HT in children. The presenting BP is usually very high and difficult to control. The chief pathophysiological mechanism underlying renovascular HT involves activation of both limbs of the renin-angiotensin-aldosterone system and depends on the presence or absence of a contralateral kidney. Renal angiography is the gold standard for diagnosis. Treatment consists of various antihypertensive drugs, angioplasty and surgery. Most affected children have a good long-term outcome.
REFERENCES