Malignant hypertension secondary to renovascular disease during infancy—an unusual cause of failure to thrive

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Abstract

An 11-month-old girl presented with a history of failure to thrive, vomiting, polydipsia and visual inattention. She was found to have malignant hypertension due to unilateral renal artery stenosis. This was successfully treated with percutaneous transluminal balloon angioplasty. Nearly 10 years following this initial presentation, she remains normotensive on no anti-hypertensive medications.

Keywords: failure to thrive; angioplasty; renovascular hypertension

Case report

An 11-month-old Caucasian girl presented with history of intermittent vomiting and irritability over the preceding 6 weeks. The parents reported no recent weight gain and this was confirmed on review of weight charts from parent held records. Her weight had been static over the preceding 5 months and had fallen from the 90th to 10th percentile [1]. She was the second child of non-consanguineous parents, born by normal vaginal delivery at 37 weeks gestation with birth weight of 3.05 kg (50th percentile) [1].

She was pale, thin and dehydrated with visual inattention and failure to fix and follow a light source but had no dysmorphic features or stigmata of neurocutaneous disease. Cardiovascular examination was normal with no murmurs or bruits. Systolic blood pressure (BP) was 230 mmHg (95th percentile for age 106–67 mmHg) [2], urinalysis showed 3+ haematuria and 3+ proteinuria, blood investigations showed haemoglobin 15.7 g/dL (10.5–13.5), sodium 127 mmol/L (135–145), potassium 3.4 mmol/L (3.5–5.0), urea 6.6 mmol/L (1.7–8.3), creatinine 49 μmol/L (18–48) and albumin 46 g/L (40–52). Following rehydration with 0.9% saline, her systolic BP improved to 170 mmHg and blood results showed haemoglobin 10.7 g/dL, sodium 139 mmol/L, potassium 2.4 mmol/L, urea 3.4 mmol/L, creatinine 30 μmol/L and albumin 25 g/L. She was commenced on labetalol infusion and systolic BP was slowly reduced to 120 mmHg over 4 days. During this period, her anti-hypertensive therapy was converted to three oral anti-hypertensive agents to maintain adequate BP control.

Visual inattention resolved within 12 h of commencing treatment. Her fundoscopy examination was normal. Echocardiography revealed severe left ventricular hypertrophy. Renal ultrasound (US) showed right kidney 5.3 cm in length with normal sonographic appearances and large left kidney, 7.3 cm in length, with increased cortical echogenicity. It was not possible to visualize renal arteries with doppler US. 99mTc dimercaptosuccinic acid (DMSA) scan reported an irregular shaped right kidney with 45% function and normal left kidney. Digital subtraction angiography (DSA) demonstrated severe right renal artery stenosis (RAS) probably secondary to fibromuscular dysplasia (FMD) with normal left renal artery and aorta (Figure 1a).

No other abnormalities involving other arterial beds were noted.

A successful right renal artery percutaneous transluminal balloon renal angioplasty (PTRA) was performed using a 3.5 mm × 9 mm coronary balloon catheter via left common...
femoral artery approach (Figure 1b and c). The patient was discharged 5 days later on two oral anti-hypertensive agents. An US scan 4 months following angioplasty demonstrated two normal kidneys of equal size (6.4 cm bilaterally). Twenty months following initial presentation, she was thriving with weight of 12.6 kg (75th–91st percentiles) and normal BP on no anti-hypertensive medications. At 9 years of age, she remains well with normal BP of 80/36 mmHg and no anti-hypertensive therapy.

Discussion

Hypertension in infants and young children almost always have an identifiable cardiac, renal or, rarely, endocrine disorder [3]. Renovascular hypertension can be defined as hypertension from obstruction to blood flow in the renal artery or its branches. Renovascular diseases (RVD) may account for 10% of causes of severe hypertension in children [4, 5] and are the third commonest cause of significant hypertension in children after renal scarring and glomerular disease. Non-syndromic causes of renovascular hypertension in otherwise well term infants include coarctation of aorta and FMD [6]. Genetic disorders associated with RVD during infancy include neurofibromatosis, Williams syndrome and tuberous sclerosis [6].

It is well recognized that hypertensive infants may present with failure to thrive and poor feeding [5], although its pathogenesis is not fully understood [5, 7]. Several case studies have shown that failure to thrive is caused by hypertension, irrespective of aetiology, good BP control leads to improved growth [5, 7]. Visual disturbance, including visual loss, has also been well described in children with hypertensive encephalopathy [8] and improves within hours of commencing treatment [9]. Other symptoms linked to hypertension include behavioural changes such as restlessness and hyperactivity [3, 10]. The wide-ranging non-specific nature of such symptoms that can be attributed to hypertension during infancy highlights the importance of including BP measurement in the routine monitoring of sick infants. Our patient had a 5-month history of failure to thrive but no recorded BP measurements. We suggest early evaluation of BP as part of initial screening is vital for such infants and young children.

RVD causing renal artery stenosis is seen in a heterogeneous group of disorders, mostly resulting from intrinsic lesions although rarely due to extrinsic compression [6]. FMD is thought to be the commonest cause during childhood [11]. Unilateral renal artery stenosis results in the hypoperfusion of the affected kidney and causes renin release, which triggers increased angiotensin II production leading to increased aldosterone production. Angiotensin II causes powerful vasoconstriction, while aldosterone increases sodium and water retention by kidneys. These effects in combination can cause persistent hypertension. Here, the combination of pressure naturesis and vomiting led to hypovolaemia contributing to hypertension as evidenced by the dramatic fall in BP following rehydration. Hypovolaemia leading to hypertension is well described in children and is thought to be due to hyper-reninaemia [3].

RVD is an important cause of severe hypertension, having potentially curative intervention and significant morbidity if not treated. It is therefore essential that investigations seek to prevent potential vascular problems being overlooked.
subtraction angiography (DSA) remains the investigation of choice [3, 12, 13]. Although less invasive other modalities (including Doppler US, Captopril DTPA scans, magnetic resonance angiography and computerized tomography angiography) are helpful, none have the sensitivity to exclude RVD [3, 13]. Newer non-invasive imaging modalities though are becoming increasingly more precise and DSA may not be needed for diagnosis in the near future for RVD involving the main renal artery.

Most children with RVD require intervention or surgical treatment. PTRA is well described for RAS in children and adults, particularly if there is a solitary stenosis [12]. In infants and young children, PTRA is not without risks meaning medical management is often considered [14]. There are a few examples of its use and success in children under 12 months of age in whom renal arterial disease was isolated, proximal and clinically stable. Six reports described infants having transluminal angioplasty following initial presentation with hypertension [15–20] (Table 1). Five had unilateral and one bilateral renal arterial disease with no other arterial vascular bed involvement. Most cases were secondary to FMD with one case associated with neuroblastoma [19]. In five, PTRA was immediately successful. Over subsequent follow-up, three children no longer required anti-hypertensive medication. One further child probably became hypertensive as he required an autotransplant 2 years following initial PTRA [17]. We found only one previous report documenting continued normotension at 14 months follow-up after PTRA.

In summary, this case of malignant hypertension secondary to unilateral renal artery stenosis was successfully treated with balloon angioplasty during infancy and remained normotensive several years following initial presentation. This case also highlights the importance of checking the BP in infants with failure to thrive. As significant proportions of patients with RVD secondary to FMD develop lesion re-stenosis and often require multiple interventions [6], follow-up throughout childhood is prudent despite early treatment success. Any recurrence of hypertension should prompt investigations to rule out re-stenosis of previously treated RVD.

Acknowledgements. Funding. The author M.D.S. acknowledges financial support from the Department of Health via the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre award to Guy’s and St Thomas’ NHS Foundation Trust in partnership with King’s College London and King’s College Hospital NHS Foundation Trust.

Conflict of interest statement. None declared.

References

Table 1. Summary of reported cases of infants with renal arterial disease treated with transluminal balloon angioplasty with reported duration of follow-up

<table>
<thead>
<tr>
<th>Author et al.</th>
<th>Uni/bilateral</th>
<th>Age at angioplasty</th>
<th>Presenting systolic BP (mmHg)</th>
<th>Outcome</th>
<th>Follow-up (in months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patterson et al. [15]</td>
<td>Unilateral</td>
<td>11 months</td>
<td>135</td>
<td>Failed</td>
<td>Surgical repair</td>
</tr>
<tr>
<td>Lee et al. [16]</td>
<td>Unilateral</td>
<td>9 months</td>
<td>186</td>
<td>Success</td>
<td>12</td>
</tr>
<tr>
<td>Estepa et al. [17]</td>
<td>Bilateral</td>
<td>11 months</td>
<td>Not specified</td>
<td>Improved*</td>
<td>24b</td>
</tr>
<tr>
<td>Takigiku et al. [18]</td>
<td>Unilateral</td>
<td>5 months</td>
<td>192</td>
<td>Success</td>
<td>8</td>
</tr>
<tr>
<td>Shinohara et al. [19]</td>
<td>Neuroblastoma with contralateral kidney with two renal arteries both with stenosis</td>
<td>5 months</td>
<td>200</td>
<td>Improved*</td>
<td>14</td>
</tr>
<tr>
<td>Daehnert et al. [20]</td>
<td>Unilateral</td>
<td>8 days</td>
<td>20 mmHg above upper limit of normal</td>
<td>Success</td>
<td>6</td>
</tr>
</tbody>
</table>

*Improved, still requiring anti-hypertensives at follow-up.

bKidney autotransplanted 2 years following initial PTRA.
Primary renal MALT lymphoma presenting with cryoglobulinaemia

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Abstract
Primary renal lymphoma is a rare clinicopathologic entity that typically presents as renal mass or renal impairment with enlarged kidneys. We describe the case of a 66-year-old woman who presented with type II mixed cryoglobulinaemic vasculitis as the first manifestation of underlying low-grade primary renal lymphoma.

Keywords: MALT lymphoma; mixed cryoglobulinaemia; primary renal lymphoma

Introduction
Kidney involvement is not uncommon in systemic lymphoma, usually occurring in patients with disseminated disease [1, 2]. By contrast, primary renal lymphoma (PRL) is a very rare clinicopathologic entity, the kidney being one of the organs normally not containing lymphoid tissue [2]. There are few studies in the literature covering the topic of PRL. PRL typically presents as a renal mass or renal impairment in the setting of enlarged kidneys, and most cases are related to aggressive types of lymphoma [3]. Low-grade lymphomas represent exceptional aetiologies of PRL. We report here the case of a 66-year-old woman who presented with normal-sized kidneys, Type II cryoglobulinaemic vasculitis and acute kidney injury due to low-grade PRL. This is the first report of cryoglobulinaemia arising on the background of PRL.

Case
A 66-year-old woman was referred to the nephrology department due to deterioration of renal function found in laboratory tests that were carried out because of weakness, oedema, dyspnoea on exertion and hypertension for the last 4 months. Her medical history was unremarkable. On physical examination, blood pressure was 180/110 mmHg, temperature 36.6°C and pulse 82 beats per minute. There was 2+ pitting oedema in the ankles and palpable purpura on both legs. Laboratory examinations revealed a leukocyte count of 5370/µL, haemoglobin 10 g/dL, platelets 90 000/µL, erythrocyte sedimentation rate 102 mm/h, urea 152 mg/dL, creatinine 3.77 mg/dL, albumin 3.2 g/dL and lactate dehydrogenase 320 U/L. Liver function tests, electrolytes and C-reactive protein were normal. Urinalysis demonstrated 60 erythrocytes per high power field, granular and hyaline casts and nephrotic proteinuria (12 g/day). Ultrasonography showed kidneys of normal size, whereas Doppler examination did not reveal blood flow abnormalities. Computed tomography of head, chest and abdomen was unremarkable. Anti-globulin test, anti-nuclear antibodies, antibodies to extractable nuclear antigens (ENAs), anti-phospholipids and anti-neutrophil cytoplasmic antibodies were negative. Complement C4 and CH50 levels were low (<1.67 mg/dL and <15 U/L, respectively), while C3 level was normal (84.4 mg/dL). Rheumatoid factor (RF) was markedly elevated at 1370 U/mL. Serum and urinary protein electrophoresis were negative; however, serum immunofixation revealed an IgM-kappa monoclonal component. Immunoglobulin measurements showed IgG 501 mg/dL, IgM 156 mg/dL, IgA 146 mg/dL, kappa-free light chains 853 mg/L, lambda-free light chains 30.5 mg/L and k/λ ratio 28:1. The patient’s serum tested positive for cryoglobulins and immunofixation of the cryoprecipitate demonstrated Type II mixed cryoglobulinaemia (MC). The cryocrit was 10% and the concentration of circulating immunocomplexes...