CASE REPORT

Renovascular hypertension: a case with atypical neurological signs

Mónica Jerónimo,[1] Teresa Dionísio,[2] Clara Gomes,[3] José Farela Neves[2]

[1]Hospital Pediátrico de Coimbra, Coimbra, Portugal
[2]Pediatric Intensive Care Unit, Hospital Pediátrico de Coimbra, Coimbra, Portugal
[3]Department of Paediatric Nephrology, Hospital Pediátrico de Coimbra, Coimbra, Portugal

Correspondence to
Dr Mónica Jerónimo,
monica.djeronimo@gmail.com

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SUMMARY

Secondary hypertension is the most frequent form of hypertension in children. Renovascular disease accounts for 5–10% of all childhood hypertension and should be suspected in the presence of severe hypertension found difficult to manage with medical therapy. Uncontrolled hypertension can lead to severe target organ damage. We describe the case of a 13-month-old baby boy with failure to thrive, recent muscular weakness of the lower extremities and irritability. Hypertension was detected and he was admitted to the paediatric intensive care unit with a refractory hypertensive emergency, despite multiple antihypertensive therapies. Bilateral renal artery stenosis was diagnosed through renal angiography and balloon dilation was performed, leading to lower blood pressure. He is currently withdrawing from antihypertensive medication, and slowly gaining weight and recovering from target organ damage. However, weakness of the lower extremities persists and he has been diagnosed with a neurogenic bladder.

BACKGROUND

Hypertension affects 1–5% of children and adolescents.[1 2] Unlike adults, whose hypertension is usually primary, most childhood hypertension is secondary to an underlying disorder.[3–5] Renovascular hypertension (RVH) disease accounts for 5–10% of all cases.[4 6 7] It is characterised by a lesion that limits blood flow to one or both kidneys, leading to an activation of the renin–angiotensin–aldosterone system (RAAS). RAAS activation results in vasoconstriction and increase in blood volume, contributing to hypertension, which is usually serious and difficult to control with medical treatment.[4 6 8] Fibromuscular dysplasia corresponds to 60% of all cases of RVH, with bilateral involvement of the renal artery in about 53–78%.[6]

Hypertension can be silent or lead to symptoms related to target organ damage (hypertensive emergency) such as behavioural changes, neurological deficits, visual changes or heart or renal failure.[5 6 9] Failure to thrive (FTT) is also described in association with hypertension.[5 10 11]

We describe the presentation, diagnosis and management of a 13-month-old baby boy with severe RVH and target organ damage secondary to bilateral renal artery stenosis. His neurological signs were severe and did not improve with blood pressure (BP) control.

CASE PRESENTATION

We report a case of a 13-month-old Caucasian boy, born from the second pregnancy of a consanguineous couple (second degree cousins). The pregnancy was uneventful and with normal fetal ultrasound scans. The child was born at term, from caesarean section, with a birth weight of 3000 g. He had normal psychomotor development and an insignificant medical history. His father had recently been diagnosed with essential hypertension. The child was followed up since he was 9 months old due to FTT, slowing of his linear growth and recent polyuria and polydipsia. Physical examination revealed weight and height below the fifth centile (7 kg and 72 cm, respectively), and weight-for-length below the fifth centile. The child's skin was pale, without achromic or café-au-lait spots, and he had malnutrition signs including decreased subcutaneous tissue on his buttocks and thin hair. Abdominal distension was present, without palpable masses, hepatomegaly or murmurs.

Laboratory results showed hypochloraemic alkalosis, hypokalaemia, hyponatraemia, hypoalbuminaemia and nephrotic proteinuria. Coeliac disease and cystic fibrosis were excluded. At the age of 13 months, the child was referred and admitted to the paediatric nephrology department with the hypothetical diagnosis of atypical hypochloraemic alkalosis (type III). During the week prior to admission, he developed muscular weakness of both lower extremities, with left lower limb paresis, loss of motor acquisitions and sustained irritability. During hospitalisation, severe hypertension was found, with a maximum value of 227/125 mm Hg (95th centile for age, gender and height: 98/54 mm Hg). Target organ damage evaluation showed left ventricular concentric hypertrophy with normal contractile function (echocardiography) and hypertensive retinopathy (fundoscopy). Cranioencephalic and spine MRI demonstrated signs of microvascular lesions compatible with medullary infarction. Given the hypertensive emergency, the child was admitted to the paediatric intensive care unit for treatment and started on an intravenous infusion of labetalol (up to 3 mg/kg/h). Partial BP control occurred in the first 24 h of admission. However, he maintained BP superior to the 99th centile and a second infusion with sodium nitroprusside (up to 4 μg/kg/min) needed to be added. Oral minoxidil, amlodipine, captopril and atenolol were progressively added to the treatment with the aim of withdrawal from intravenous infusions. However, the child maintained an elevated BP despite maximum doses of all oral antihypertensive drugs. Starting the fourth day of admission, he presented with acute renal failure with a maximum

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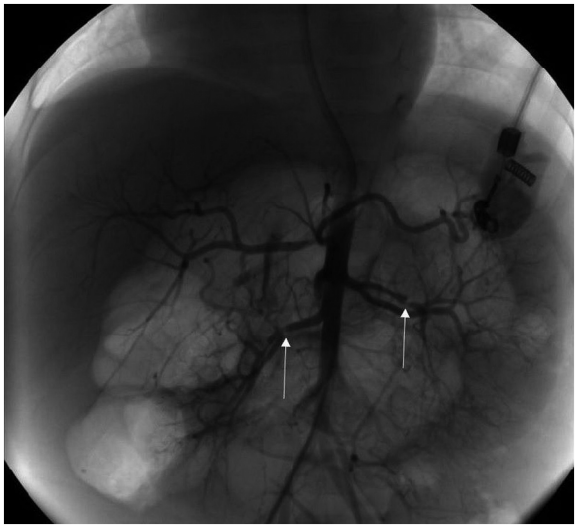

Figure 1 Renal angiography revealing bilateral renal artery stenosis (*arrows*).

urea of 13.4 mmol/L and creatinine of 116 µmol/L (glomerular filtration rate: 24.8 mL/min/1.73 m^2). Furosemide infusion was added due to anasarca.

Other investigations showed hypochloraemic metabolic alkalosis, hyponatraemia (134 mmol/L), hypokalaemia (2.8 mmol/L), hypercholesterolaemia and hypertriglyceridemia without hypoalbuminaemia. Urinalysis demonstrated nephrotic proteinuria, microscopic haematuria and glycosuria, and there was increased activity of plasmatic renin (>500 µUI/mL with hyperaldosteronism (150 pg/mL)). Renal ultrasound revealed a larger left kidney with an apparent posterior mass and poor parenchyma-sinus differentiation, confirmed by an abdominopelvic CT scan and MRI. Renal Doppler ultrasound was compatible with right renal artery stenosis. A biopsy of the posterior segment of the left kidney was performed after reasonable BP control. Anatomopathological examination described a generalised obliterans arteriolopathy and chronic interstitial nephritis, compatible with sustained hypertension. Bilateral renal artery stenosis was found in the renal angiography with two areas of preocclusive stenosis of the right renal artery and a stenosis of the superior branch of the left renal artery (figure 1). Bilateral angioplasty with balloon dilation was performed with favourable response (figure 2). A rupture of two collateral branches of the left renal artery occurred during the procedure, which was successfully treated by transcatheter embolisation with microcoils.

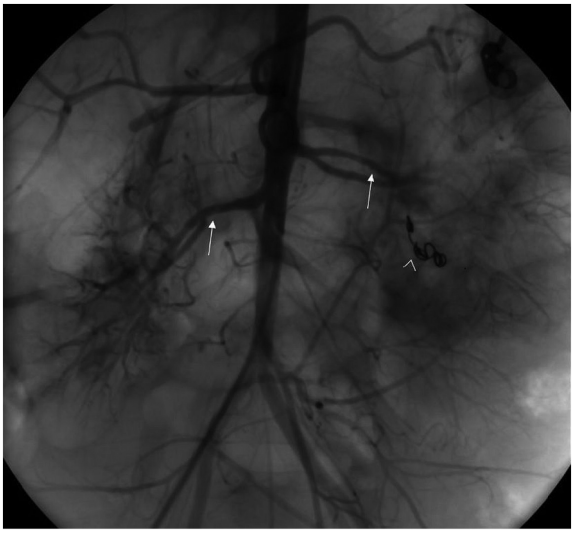

Figure 2 Bilateral renal artery stenosis solved after angioplasty with balloon dilation (*arrow*). A rupture of two collateral branches of the left renal artery occurred during the procedure, which was successfully treated by transcatheter embolisation with microcoils (*arrowhead*).

High plasmatic levels of renin and aldosterone were measured within the renal vein (1495 µU/mL and 439 pg/mL, respectively), without a difference between left and right renal veins. After the procedure, a substantial decrease in BP occurred, allowing for the suspension of the intravenous infusions a few hours later. However, the child maintained BP above the 95th centile, requiring maintenance of the oral prescriptions (amlodipine, minoxidil, captopril and atenolol). An improvement in irritability and weight recovery occurred during the following weeks after the procedure. About 6 weeks later, renal Doppler ultrasound scan revealed worsening of the right renal artery stenosis and renal artery angiography was repeated. Stenosis narrower than 50% was found and, consequently, dilation was not performed.

Renal scintigraphy with Tc-99m dimercaptosuccinic acid was also performed, which revealed parenchymal damage mainly in the left kidney, with a functional amputation of its posterior segment. Differential kidney function was 63% (right) vs 37% (left).

Neurological deficits persisted, with spastic paraparesis of the inferior limbs and pyramidal signs, probably secondary to medullary infarction. Proteinuria and haematuria gradually reduced, with normal values from the 40th day after angioplasty. Dyslipidaemia resolved on the 17th day after the procedure. Renin and aldosterone levels also reduced gradually with normal aldosterone levels returning on the 40th day after angioplasty. However, renin levels remained high (183 µU/mL) 4 months after the procedure. Renal function was normal from the second day after angioplasty.

The child was discharged 43 days later, under treatment with amlodipine, minoxidil, atenolol and captopril.

OUTCOME AND FOLLOW-UP

The child's BP gradually reduced, with the majority of evaluations below the 95th centile. He is still medicated with the four antihypertensive drugs 4 months after the first angiography. His left ventricular hypertrophy and retinopathy are gradually improving. He is recovering growth and under a rehabilitation programme with a slight improvement of mobility. A neurogenic bladder was subsequently found for which he is under treatment with oxybutynine. He is followed in the nephrology, neurology, cardiology and ophthalmology outpatient clinics.

DISCUSSION

Renal artery stenosis is a rare but important cause of childhood hypertension. Early diagnosis is essential because adequate treatment can prevent target organ damage.[3 5] In the case described, RVH diagnosis was late and difficult because of its presentation with FTT, slowing of linear growth and atypical neurological signs.

This child had FTT and hypochloraemic alkalosis, which initially evoked the hypothesis of Bartter or Gitelman syndrome. These two syndromes can present with hypochloraemic alkalosis, hypokalaemia and FTT.[12] However, they were less likely after taking into account the hypertension this child presented

and the subsequent diagnosis of bilateral renal artery stenosis. Cystic fibrosis can also cause FTT. Metabolic alkalosis and electrolyte depletion may also occur in these patients.[13 14] Cystic fibrosis was excluded by a negative sweat test.

RVH has been described as a rare cause of FTT, and probably occurred in this case, since growth recovery occurred after improvement of BP levels.[5 10 11]

High BP values must be confirmed and taken into consideration. Children with severe hypertension can present with severe neurological signs such as headache, facial palsy, acute hypertensive encephalopathy or cerebrovascular incidents.[5 9 15] In this case, there were behavioural changes (irritability), spastic paraparesis and neurogenic bladder. The cranioencephalic and spine MRI showed microvascular lesions compatible with medullary infarction, which probably occurred due to severe hypertension. Paraparesis and neurogenic bladder, caused by medullary infarction, are probably a consequence of vascular injury and haemodynamic instability due to severe hypertension.

The medullary infarction lesions are the likely origin of this patient's neurological deficits (spastic paraparesis and neurogenic bladder).

An activation of the RAAS by the damaged kidney probably occurred, with subsequent hypokalaemia, hypervolaemia and hypertension. Hypervolaemia led to an activation of the atrial natriuretic peptide and consequent pressure natriuresis by the contralateral kidney as well as RAAS inhibition, creating a vicious cycle. Pressure natriuresis caused a decrease in intravascular volume, stimulating thirst and the release of antidiuretic hormone. All these mechanisms associated with the sodium depletion resulting from natriuresis contributed to hyponatraemia. Proteinuria, haematuria and glycosuria can also be explained by this hyperfiltration state.[16–18] Although a bilateral stenosis was diagnosed in this case, it is possible that, during the initial phase, there was a smaller commitment of one of the kidneys, creating the mechanism described above.

The literature reports limitations of renal Doppler ultrasound scanning in diagnosing RVH.[3 6 7 19 20] In the present case, it provided the diagnostic suspicion of right renal artery stenosis, although without identifying bilateral stenosis. Renal angiography is the most accurate method for assessment of suspected RVH and allows for treatment with renal angioplasty during the same procedure.[3 6] Measurement of renal vein renin and aldosterone concentrations is also useful to diagnose RVH, especially when the stenosis is bilateral.[6]

Regarding pharmacological therapy, ACE inhibitors and angiotensin receptor blockers must be carefully used since they provoke efferent glomerular arteriole dilation, thus reducing filtration pressure. In cases with bilateral stenosis, they can induce an important decline in glomerular filtration rate with subsequent acute renal failure, as occurred in this case.[6 20 21] Yet, it was the most effective drug. Renal function should be assessed frequently when these drugs are used.[6 21]

Percutaneous renal angioplasty may be the first-line intervention to treat childhood RVH, with a cure rate between 22% and 59% and improvement in 22–74%.[22–24] Angioplasty results are also less satisfactory in children than in adults, probably due to the smaller diameter of the vessel and the higher response of the immature vasculature to growth factors.[8 23] Thus, there is a higher risk of restenosis, as occurred in this case. Renal artery stenting in children is controversial and rarely used, since it is associated with non-negligible restenosis, and its long-term results are not yet fully known in this age group.[6 21 23 24]

In this case, percutaneous angioplasty performed during angiography allowed the diagnosis and at the same time enabled renal artery dilation. An important improvement of BP was registered, although with sustained need for multiple antihypertensive drugs. Renal artery restenosis occurred, which led to repeating the procedure.

Surgery is reserved for RVH cases resistant to previously described treatments.[6] With this case report, we intend to emphasise an unusual RVH presentation with FTT, slowing of linear growth and atypical neurological signs resulting from central nervous system damage. Renal angiography was the decisive diagnostic method and renal artery angioplasty the preferential treatment. However, this child currently has important neurological deficits and requires multidisciplinary follow-up. This case highlights the importance of BP measurement in FTT. Proper management of RVH and prevention of its complications depend on prompt recognition and treatment.

Learning points

- Secondary hypertension is the most common form of hypertension in childhood. It may be associated with failure to thrive.
- Renovascular disease is an important cause of severe childhood hypertension.
- Renal angiography is the gold standard method for assessment of suspected renovascular hypertension.
- Angioplasty is usually required, as renovascular hypertension is usually refractory to pharmacological treatment.
- Hypertension can lead to severe target organ damage, which can be difficult to recover even after blood pressure normalisation.

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