



# Hypertensive crisis as the first manifestation of renal disease in children and adolescents: a report of three cases and review of the literature

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## Abbreviations:

BP = blood pressure  
CR = creatinine  
DMSA = dimercaptosuccinic acid  
DTPA = diethylene triamine penta-acetic acid,  
ECG = electrocardiogram  
LVH = left ventricular hypertrophy  
MRA = MR angiography

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## Abstract

**Introduction:** Hypertensive crisis is a life-threatening condition, defined as severe hypertension complicated with acute target-organ dysfunction (mainly neurological, renal or cardiac). It rarely occurs in childhood and most children and adolescents who presents with hypertensive crisis symptoms have secondary hypertension, mainly of renal etiology.

**Case reports:** We present the cases of three children with severe hypertension of different renal etiology who presented with the characteristic features of hypertensive emergency. Case 1 is a 11-year-old girl with reflux nephropathy who at admission had blood pressure (BP) as high as 250/200 mmHg. She was lethargic, with headache, vomiting and a 3-month history of weight loss. Case 2 is a 13-year-old boy with renal artery stenosis who had clinical presentation of generalized tonic-clonic seizures and BP 220/150 mmHg. Case 3 is a 9-year-old boy with chronic renal insufficiency of unexplained etiology and BP as high as 220/135 mmHg. This patient, like two others, presented dominantly with symptoms of hypertensive encephalopathy, as well as signs of renal damage. All three patients have documented hypertrophic cardiomyopathy. In the patient who had renal artery stenosis, the removal of his dysplastic atrophic right kidney failed to normalize his blood pressure.

**Conclusion:** We discuss the cases of unrecognized long-standing hypertension, with progression to malignant hypertension, as the first manifestation of renal disease – two with renal parenchymal disorders and one with renovascular disease. Hypertension is underdiagnosed in children and the purpose of these case reports is to raise awareness about it and point to the importance of routine careful measurement of blood pressure in pediatric patients.

## INTRODUCTION

Hypertension is frequently undiagnosed in pediatric population for several reasons (1, 2). Diagnosis of hypertension in children is complicated because normal and abnormal blood pressure (BP) values vary with age, sex and height, and it is therefore difficult to have all these numbers in mind. High BP in children is defined as BP values

that are at or above the top 5% of the normal BP range ( $\geq 95^{\text{th}}$  percentile) (3). Evaluation of BP measurement in a child first requires determination of the child's height percentile, and then a comparison of the child's BP level with the childhood BP tables according to sex, age and height percentile of the child. Furthermore, compared with adults, there are more technical issues in accurate BP measurement such as the appropriate BP cuff size and difficulty with auscultation in noncompliant children. Actually, auscultation is the preferred method for BP measurement. Automated oscillometric instruments are not recommended in routine care. These devices are commonly used in large pediatric clinics due to convenience, but they should be validated in pediatric population and require trained staff. It is recommended that BP measurements obtained by oscillometric devices that exceed the 90<sup>th</sup> percentile should be repeated by auscultation (2, 3, 4). Moreover, high BP values are generally dismissed as inaccurate.

As in adults, mild to moderate hypertension in children and adolescents can be asymptomatic or may involve subtle symptoms (headache, epistaxis), and changes in behavior or school performance. However, secondary causes of hypertension are much more common in children than in adults. Although secondary forms of hypertension commonly cause severe hypertension, they should always be considered when hypertension is diagnosed in children, because unrecognized long-standing hypertension inevitably leads to end-organ damage and may cause hypertensive crisis, a life-threatening condition.

Hypertensive crisis, as emergency or urgency, is associated with severe hypertension. Hypertensive emergency is distinguished from hypertensive urgency by the presence of acute end-organ dysfunction in the history, physical examination or investigations, rather than only by the high level of blood pressure (5).

Hypertensive emergency is defined as severe hypertension complicated with acute target organ dysfunction, mainly neurological, renal or cardiac. It rarely occurs in childhood and most children and adolescents who present with hypertensive crisis symptoms have secondary hypertension, mainly of renoparenchymal or renovascular in origin (4, 6). Of all secondary hypertension cases, renal parenchymal disease accounts for at least 75% and renovascular disease for another 10% of cases (2). Less common causes of secondary hypertension include endocrine disorders, cardiovascular disease (eg. coarctation of the aorta) and some monogenic inherited forms of hypertension (e.g. Gordon's syndrome, Liddle's syndrome, glucocorticoid-remediable aldosteronism, apparent mineralocorticoid excess, mineralocorticoid receptor hypersensitivity syndrome and hypertensive forms of congenital adrenal hyperplasia) (2, 4).

We discuss the cases of unrecognized long-standing hypertension, with progression to malignant hypertension, as the first manifestation of renal disease – two cases with renal parenchymal disorders and one with renovascular disease.

## CASE REPORTS

### Case 1

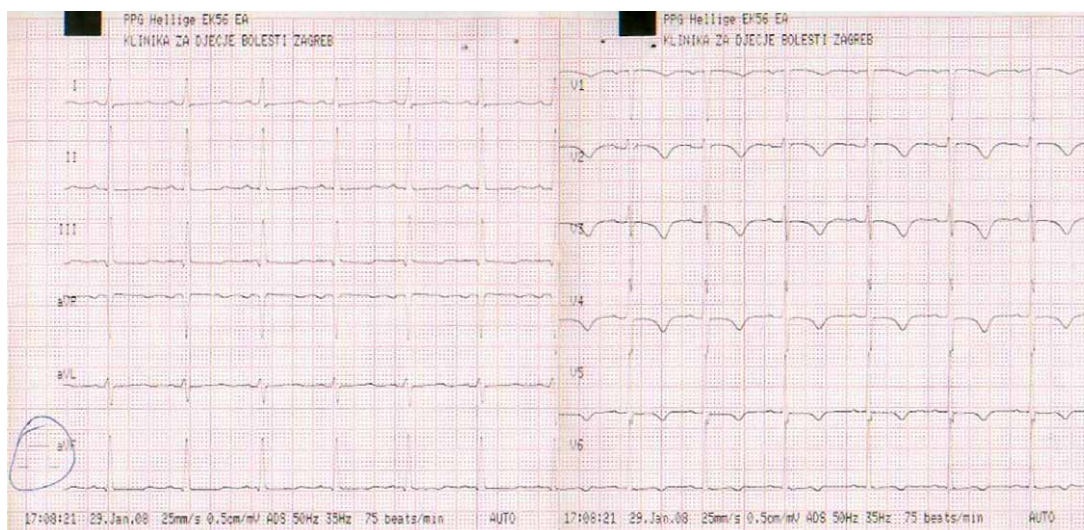
A 11-year-old girl presented with headache, nausea, vomiting and anorexia – she lost 8 kg in the last 3 months. She was complaining of blurring and diplopia. There was a preceding history of recurrent febrile urinary tract infections. She had also complained of occasional headache for last 2 yrs, intensified during last 3 months.

On admission to our hospital her blood pressure was as high as 250/200 mmHg. She was lethargic, atactic, dislalic, with headache, vomiting and had visual impairment (criss-cross vision). Laboratory data revealed elevated serum creatinine (184  $\mu\text{mol/L}$ ) and urea (13.1 mmol/L), microscopic hematuria and proteinuria (4 g/day), with creatinine clearance of 28 mL/min/1.73 m<sup>2</sup>. Serum electrolytes (Na, K), immunologic work-up including serum complements (C3 and C4), anti-nuclear antibody (ANA), anti-double-stranded DNA, antineutrophilic cytoplasmic antibody (ANCA) and hormonal status (thyroid hormones, catecholamines, vanilmandelic acid, renin, aldosterone, cortisol) were within normal limits. Fundoscopy revealed grade IV hypertensive change, with hemorrhage, cotton-wool exudates and papilledema. Chest x-ray showed cardiomegaly (Figure 1). Electrocardiogram revealed left ventricular hypertrophy (Figure 2), while echocardiography confirmed concentric symmetric LVH (Figure 3). Kidney ultrasound showed 2 cm smaller right kidney compared to the left one, with a hyperechogenic parenchyma. There were no Doppler criteria for renal artery stenosis. Left vesicoureteral reflux grade III became obvious with voiding cystourethrogram. DMSA renal scintigraphy demonstrated scars in both kidneys. CT scan of the brain showed cerebellar ischemic insult (Figure 4).

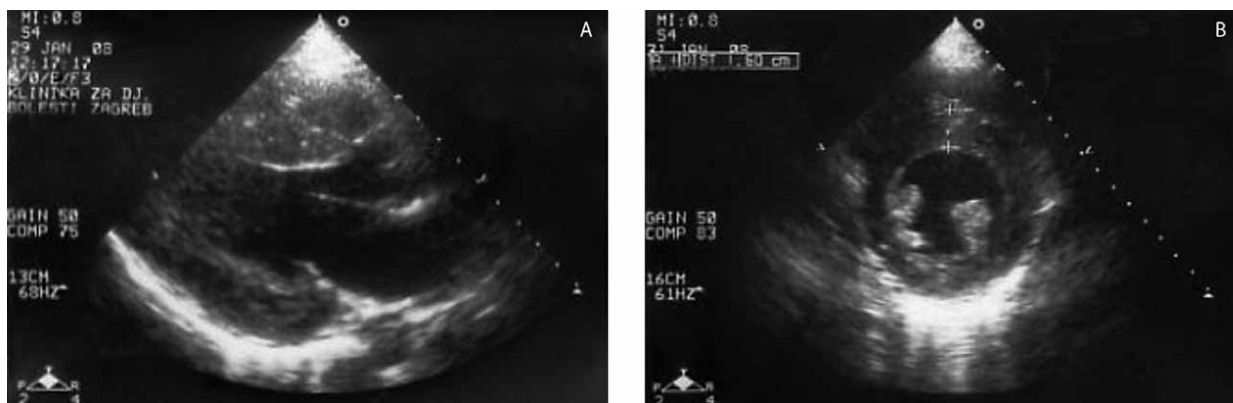
This case of a girl with past medical history of recurrent urinary tract infections is very suggestive for vesicoureteral reflux, with possible development of reflux nephropathy, which was confirmed with appropriate radiological examinations. Because of her long-standing headache, it is likely that chronic unrecognized and un-



**Figure 1.** Chest x-ray of Case 1 patient with marked cardiomegaly.



**Figure 2.** Electrocardiogram (ECG) of Case 1 patient with positive criteria for left ventricular hypertrophy (LVH), the most prominent of them are: high QRS voltages in favor of the left ventricle (tracing with one-half standardization – 1 mV=5 mm), and inverted T waves in leads V5 and V6.



**Figure 3.** Echocardiogram of Case 1 patient with left ventricular hypertrophy: a) parasternal long axis view (diastolic interventricular septal thickness – IVSd=1.9 cm, diastolic left ventricular posterior wall thickness – LVPWd=1.7 cm); b) parasternal short axis view



**Figure 4.** CT scan of the brain of Case 1 patient with marked cerebellar ischemic insult (a tiny square points to it).

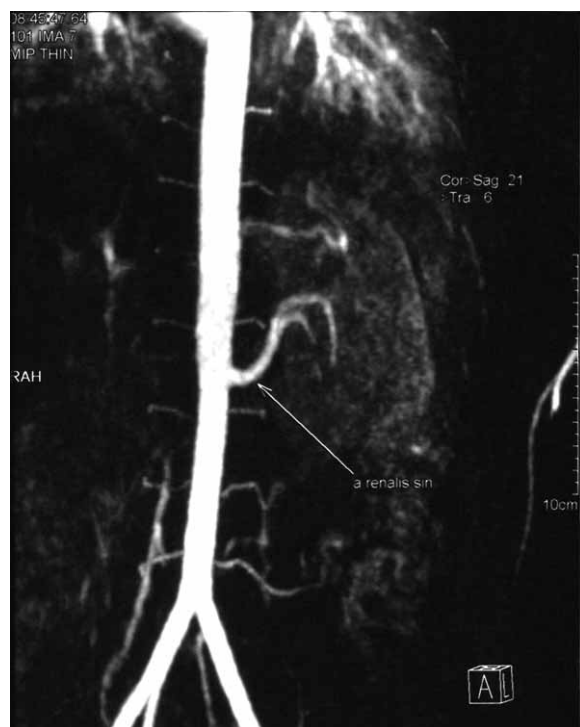
treated hypertension due to reflux nephropathy led to hypertensive emergency, with completely developed clinical presentation of acute end-organ dysfunction.

**Case 2**

A 13-year-old boy had headache, photophobia and vomiting for past 2 months, which culminated in grand mal seizures and admission to hospital, when measured BP was 220/150 mmHg. There was a history of photo-induced seizures 2 yrs ago. After cessation of seizures, physical examination, except for high BP, was unremarkable; abdominal bruit was not heard.

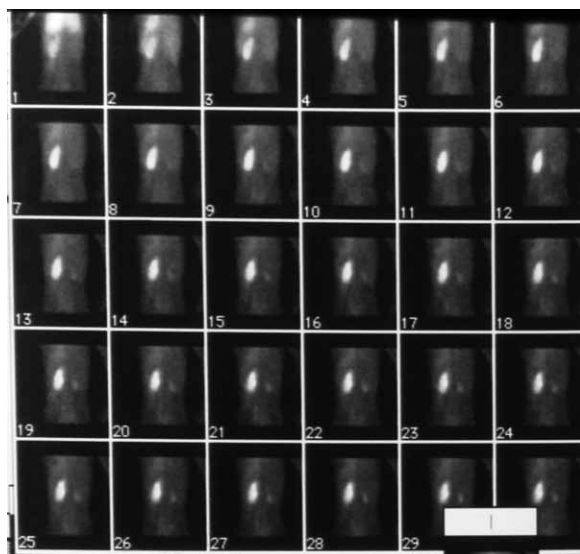
Regarding laboratory tests, serum urea level was elevated (9.9 mmol/L), the same as creatinine (140 μmol/L). Proteinuria of 750 mg/day and CR clearance of 76.4 mL/min/1.73 m<sup>2</sup> were measured. Kidney ultrasound showed small hyperechogenic right kidney with hypoplastic renal artery and, with color Doppler study, evidence of right renal artery stenosis. MR renal angiography veri-





**Figure 5.** MR renal angiography of Case 2 patient with well visible left renal artery and filiformed (barely visible) right renal artery.

fied filiformed right renal artery, without evidence of right kidney arterial phase (Figure 5). On DTPA-renal scan, GFR was 95 mL/min/1.73 m<sup>2</sup>; >95% belonged to the left kidney, right kidney was small, with poor accumulation of DTPA (Figure 6). On fundoscopy, there were no pathological findings. Of cardiac tests, ECG showed signs of left ventricular hypertrophy and echocardiogram confirmed it. According to very low function



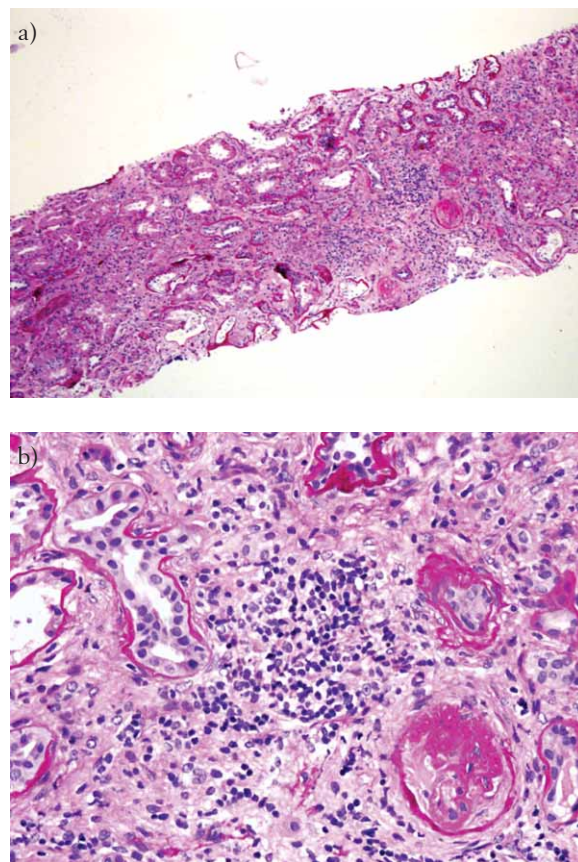
**Figure 6.** DTPA-renal scan of Case 2 patient with marked left-to-right asymmetry as the consequence of poor right kidney's DTPA accumulation.

of his dysplastic atrophic right kidney, nephrectomy was performed, but the procedure failed to normalize his blood pressure.

### Case 3

A 9-year-old boy had headache, vomiting, fatigue and polydipsia during the previous year. There was a preceding history of omphalocele surgery in the neonatal period. In the family history, a few members had high blood pressure, no one was on dialysis. At admission to our hospital he had predominant symptoms of hypertensive encephalopathy, as well as signs of renal damage.

On physical examination, his BP was as high as 220/135 mmHg; he was tremorous, with hyperpigmented yellowish skin. According to age and sex, his body height was on 10<sup>th</sup> percentile, and his body weight was on the 5<sup>th</sup>. Laboratory data revealed anemia, metabolic acidosis with elevated creatinine (289 μmol/L) and urea (23.0 mmol/L). He had elevated serum phosphorus and normal serum potassium. Urinalysis showed isostenuria, with normal urine sediment. Fundoscopy revealed papilledema. He had documented hypertrophic cardiomyopathy with ECG and echo exam. Renal ultrasound sho-



**Figure 7.** Light microscopy with histopathological findings of Case 3 patient's kidney biopsy; interstitial fibrosis and mononuclear (ly.) infiltration, tubular atrophy, and prominent glomerulus with fibrous changes: a – 100x enlargement, PAS staining, b – 400x enlargement, PAS staining

wed hyperechogenic parenchyma in both normal size kidneys. Kidney biopsy was performed. Light and IF microscopy (there were no glomeruli for electronic microscopy), showed end-stage renal disease with similar chronic changes in tubules, interstitial tissue and glomeruli which showed extensive global sclerosis. The histopathological findings failed to confirm whether the primary process was in the glomeruli, or in tubules (Figure 7).

## DISCUSSION

Hypertensive crisis is defined by elevated blood pressure accompanied by acute target-organ damage. Generally, it is uncommon in children, but it represents a potentially life-threatening medical emergency and requires immediate blood pressure reduction in intensive care unit to prevent or limit target-organ damage. Most children with hypertensive crisis have an underlying secondary cause for hypertension that is usually renoparenchymal (Case 1 and Case 3), or renovascular (Case 2) in origin. Medical history and physical examination should focus on symptoms and signs of end-organ injury. In a study of Deal *et al.* (7), of 110 children with hypertension requiring emergency management, hypertensive retinopathy was present in 27%, hypertensive encephalopathy in 25%, convulsions in 25%, left ventricular hypertrophy in 13%, facial palsy in 12%, visual symptoms in 9% and hemiplegia in 8% of children. Hypertensive crisis in children, compared with adults, most commonly presents with signs and symptoms of hypertensive encephalopathy – as in all our three cases, which include headache, nausea and vomiting, followed by severe headache, confusion, visual symptoms, somnolence, stupor, seizures, focal neurologic deficit and coma (3). Hypertensive encephalopathy may also result in cerebral infarction or hemorrhage, although this is more commonly seen in adults. Our Case 1 had cerebellar ischemic insult due to malignant hypertension (Figure 4).

Because of the development of normative blood pressure levels throughout childhood, the ability to identify children who have abnormally elevated blood pressure has improved. The evaluation of hypertension in childhood has continued to evolve over the past 4 decades. The turning point in the field of childhood hypertension was publication of the consensus guidelines contained in the 2004 »Fourth Report« (3, 8). Current recommendation is that all children from the age of 3 years have their blood pressure measured at each medical encounter (3, 4, 9). Younger children also require blood pressure measurement if they have a history of prematurity, heart or kidney disease, or other conditions that could alter blood pressure. Recurrent urinary tract infections, which are common in children and often associated with vesicoureteral reflux, are certainly among them (3). Accurate diagnosis of urinary tract infections and vesicoureteral reflux is important because of their association with renal damage and scarring. In year 1973, the term reflux nephropathy was first used to describe the renal damage caused by vesicoureteral reflux (10). The prevalence of hypertension in patients with reflux nephropathy is heteroge-

neous and varies among studies from 3 to 27% (11-14). It is well-known that renal scarring has a key role in the pathogenesis of hypertension (15, 16). Thus, it is important to realize that early detection of reflux nephropathy (Case 1) and long-term management of reflux can prevent hypertension, as well as its complication – hypertensive crisis (17).

Renovascular hypertension causes 5-10% of all childhood hypertension occurrence (18, 19). Children with renovascular hypertension often have evidence of end-organ damage due to very high and long-standing elevated blood pressure. Up to two thirds of these children have evidence of left ventricular hypertrophy, almost 60% have hypertensive retinopathy, and 10% have renal dysfunction (20). Our Case 2 had two of these conditions: left ventricular hypertrophy and renal dysfunction. Children with very high blood pressure suspected of renovascular hypertension can be investigated with non-invasive technique, such as renal-vessel Doppler ultrasound, CT or MR angiography (MRA), but digital subtraction angiography (DSA) is still the gold standard (21, 22). In Case 2 we diagnosed right renal artery stenosis with Doppler ultrasound and MRA and confirmed very poor (<5%) function of the right kidney with DTPA scintigraphy. Treatment options for renovascular hypertension include antihypertensive drugs, interventions such as percutaneous transluminal angioplasty, with or without stenting, and surgical procedure where children may benefit. Surgical procedure includes nephrectomy, renal artery reimplantation, arterial reconstruction with autologous or synthetic grafts and autotransplantation (23). Nowadays, indication for nephrectomy is a small, poorly functioning kidney that causes hypertension (20, 24, 25), and this was the case with our Case 2 patient. Unfortunately, the procedure failed to normalize his blood pressure, because renovascular hypertension is sometimes a progressive disease (23).

Case 3 is a patient whose clinical symptoms (polydipsia, fatigue, cephalgia) and laboratory findings (anemia, normal urine sediment, isostenuria and renal insufficiency), were, according to kidney biopsy, suggestive of chronic interstitial disease of unknown etiology. Chronic renal insufficiency with consequential long-standing hypertension progressed to hypertensive emergency, where symptoms of hypertensive encephalopathy were dominant.

## CONCLUSION

Hypertension is underdiagnosed in children and the purpose of these case reports is to raise the awareness. The aim of the diagnosis and treatment of hypertension is prevention or reduction of chronic end-organ damage. Early, appropriate diagnosis is important because established evaluation guidelines and effective treatment for abnormal blood pressure are available. Thus, it seems reasonable that improved diagnosis and treatment should also lead to a reduction in the incidence of hypertensive emergencies because any disorder that causes hyperten-

sion can give rise to a hypertensive emergency. Despite advances in novel imaging modalities and despite the genetic verification of selected forms of hypertension, the basic requirements for detecting and evaluating the hypertensive youth remain a thorough history and physical examination.

These cases of hypertensive crisis, as a medical emergency that still occurs in children, also enhance the importance of routine careful measurement of blood pressure in all pediatric patients, especially if risk factors for its development are present (26, 27). In children with suspected hypertension, the underlying secondary causes should be excluded and appropriate therapy and procedures should be applied.

Hypertension needs to be recognized to prevent the development of end-organ damage and its possible progression to hypertensive crisis.

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