Hyponatremic Hypertensive Syndrome (HHS) in Children Presenting as Malignant Hypertension: Case Report

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Abstract:

**Background:** The combination of hyponatremia and renovascular hypertension is called the hyponatremic hypertensive syndrome (HHS). Malignant hypertension as a presentation has been reported in adults with HHS but is rare in children. **Case Presentation:** Two children presented with seizures due to malignant hypertension and were on investigation found to have HHS. Patient 1: An eighteen month-old male presented with drowsiness, sudden onset status epilepticus and blood pressure of 210/160. The electrolytes on admission revealed sodium of 120 mEq/L and potassium of 2.1 mEq/L. The peripheral renin activity (PRA) was 172 ng/ml/min (normal 3-11 ng/ml/min) and serum aldosterone level was 91 ng/dl (normal 4 to 16 ng/dl). Patient underwent angioplasty with no success, followed by surgical correction. Two years since the diagnosis, the blood pressure is controlled with labetolol and amlodipine (at less than sixth of the pre-operative dose). The PRA is 2.4 ng/ml/min and aldosterone 15.5 ng/dl. The child had not only had three renal arteries on left but all of them were stenosed which to best of our knowledge has not been described. Patient 2: A seventeen-year-old female was admitted to pediatric intensive care unit with seizures and a blood pressure of 150/110. The PRA was 29 ng/ml/min and an aldosterone was 54 ng/dl. Her serum sodium was 128 mEq/L and potassium was 2.1 mEq/L. Her blood pressure was well controlled with intravenous labetolol followed by oral. No etiology could be established for hypertension because of failure of the patient follow up. **Conclusion:** As uncommon as hyponatremic hypertensive syndrome with malignant hypertension maybe in adults it is under-reported in children and purpose of this series is to raise its awareness.
**Background:**

The combination of hyponatremia and renovascular hypertension is called the hyponatremic hypertensive syndrome (HHS) [1-4]. The majority of patients reported have been elderly, asthenic females, and in most the underlying renal artery pathology was atherosclerosis [5]. Patients with HHS present with central nervous system like headache, confusion, and may also have polydipsia, and polyuria [1, 5, 6]. Malignant hypertension (HTN) as a presentation has been reported in adults with HHS but is rare in children beyond infancy with few reports [6-8].

With renal artery stenosis (RAS) renin secretion is increased resulting in high circulating angiotensin II (A-II) levels, leading to HTN and hyperaldosteronism resulting in pressure natriuresis [5]. We report two children presenting with seizures due to malignant HTN and subsequently found to have HHS. As uncommon HHS maybe as in adults it maybe under-reported in children as well.
Case Presentation:

Case 1: An eighteen month-old male presented with drowsiness, sudden onset status epilepticus and blood pressure (BP) of 210/160. Initially attempts were made to control seizures with anti-seizure medication with no success. After starting nitroprusside drip and gradual decrease of BP the seizures stopped. The patient by then had pinpoint pupils and little spontaneous movement. The renal sonogram was normal. The magnetic resonance imaging (MRI) showed extensive intra-cerebral hemorrhage and possible infarcts. A magnetic resonance angiogram (MRA) of the kidneys revealed diminished blood flow to the left kidney with at least two stenotic arteries (Figure 1). The electrolytes on admission revealed a sodium of 120 mEq/L and potassium of 2.1 mEq/L. The peripheral renin activity (PRA) was 172 ng/ml/min (nl 3-11 ng/ml/min) and serum aldosterone was 91 ng/dl (normal 4 to 16 ng/dl). His serum creatinine was 0.6 mg/dl. His weight was 8.6 kg (< 5th percentile) and height was 80 cm (10th percentile) and head circumference was 48.5 cm (25-50th percentile).

The patient remained on ventilator for a week. Initially rehabilitation potential was discussed but as blood pressure was very gradually lowered by 10 mm of Hg per day the toddler showed continued improvement in cortical function. After a week the patient was able to breathe spontaneously, nitroprusside was tapered off, and BP was controlled with intravenous (IV) labetolol and oral amlodipine was added later. The 2-D echo cardiogram showed severe concentric left ventricular hypertrophy (LVH). A nuclear renal scan done with 0.1 mg of IV enalaprilat resulted in decrease in of BP from 150/110 to 90/60 mm of Hg and was accompanied by ST wave changes on EKG suggestive of
cardiac ischemia. The result for RAS was inconclusive as following drop in BP as the radiotracer clearance from both kidneys completely ceased. Prior to IV enalaprilat the left kidney contributed 30% of overall function.

The patient underwent a renal angiogram (Figure 2) along with percutaneous renal angioplasty. The angiogram revealed three small renal arteries of 1 mm caliber each with stenosis on left and a normal single right renal artery. Angioplasty was attempted but the vessel would not dilate. After prolonged discussions with the patient’s family a surgical correction was planned. Prior to surgical correction the patient was on oral labetolol 125 mg orally twice a day (~25 mg/kg/day) and amlodipine 5 mg/day (0.5 mg/kg/day).

The surgical correction of triple RAS on the left kidney was performed ex-vivo while the kidney was in an ice-bath (Figure 3). Aorto-renal bypass was performed to the three renal arteries using a branched internal hypogastric artery graft. Postoperatively, the BP was controlled with labetolol and amlodipine that were gradually tapered.

Now 18 months since the surgery and 2 years since the initial presentation he is on labetolol 25 mg twice a day (current weight 14 kg; 3.5 mg/kg/day) and amlodipine 1.25 mg/day (0.08 mg/kg/day). The dose is approximately a sixth of pre-operative one. His BP is currently in the range of 100-110/ 50-60. The PRA is 2.4 ng/ml/min, aldosterone is 15.5 ng/dl and the serum creatinine is 0.2 mg/dl. His LVH has disappeared, MRI of brain has normalized, and his milestones have caught up to age appropriate levels. A nuclear renal scan done 18 months post-operatively shows that the left kidney now contributes 40% of the total function.
Case 2: A seventeen-year-old female in juvenile detention started to develop headaches. She lost consciousness and had incontinence of bladder and bowel. She was noted to have twitching of right lower limb and was transported to hospital. On admission to pediatric ICU she continued to have seizures and her BP was noted to be 150/110. She was diagnosed to have malignant HTN as no other etiology for seizures could be established and she was started on IV labetolol. She had no prior history of HTN. Her urine toxicology screen was negative. The investigations revealed a PRA of 29 ng/ml/min and an aldosterone of 54 ng/dl. Her serum sodium was 128 mEq/L and serum potassium was 2.1 mEq/L. The initial serum creatinine was 1 mg/dl but decreased to 0.8 mg/dl 48 hours later after control of HTN. The therapy was switched to oral labetolol and an angiogram was planned. The patient was discharged from hospital with good BP control pending renal angiogram and other investigations. She was lost to follow up despite best efforts therefore no etiology for her HTN could be confirmed, though RAS was strongly suspected.
Discussion:

The combination of hypertension and hyponatremia can be observed in a number of disorders including renal failure, renin-secreting tumors, and RAS [5, 7]. Renal ischemia due to RAS results in increased renin secretion, resulting in high circulating A-II, which raises BP and stimulates aldosterone resulting in pressure natriuresis [1, 9, 10]. This combination of hypereninemic hypertension with hyponatremia is called HHS [1-4]. In adults HHS presenting with malignant HTN has been more commonly reported [5] but in children beyond neonatal age is rare [6-8]. The purpose of our case series is increase awareness of HHS presenting with malignant HTN in children.

In our series the toddler clearly had renovascular HTN and in the teenager no etiology could be confirmed because of lack of follow up. The 17-year old was unlikely to have essential HTN. She had no prior history of HTN, and the likelihood of presenting with CNS symptoms due to malignant HTN is rare in children with essential HTN. Given the hypereninemia, hyponatremia, hypokalemia and the age of the patient, RAS due to fibro-muscular dysplasia (FMD) is most likely etiology of HTN [11, 12]. The important finding in both of the cases is elevated renin levels that are the pathognomonic finding in HHS [5, 6, 13]. The combination of renin induced HTN and hyponatremia results in HHS irrespective of the etiology.

The renal ischemia leads to a sudden rise in arterial pressure that can induce a pressure natriuresis through the normal kidney, leading to volume depletion and further renin release from the ischemic kidney [5, 6, 13]. Potassium deficiency from hyperaldosteronism may further stimulate renin secretion and intensify the vicious circle. The hyponatremia itself is presumed to result primarily from stimulation of thirst and
antidiuretic hormone release [3, 9, 10]. Direct renal actions of A-II to retain water in excess of sodium may also contribute.

In some cases with RAS an option is to remove the affected kidney as cure for HTN [14, 15]. We did consider the option in our toddler patient but with 30% function in the affected left kidney every attempt was made to salvage it. The incidence of triple renal artery in one kidney is about 1% of population [16, 17]. The toddler in our series had not only had three renal arteries on left but all of them were stenosed which to best of our knowledge has not been described in an eighteen month old. The failure of angioplasty because of ~1 mm caliber of each of the vessels is not surprising.

The step-wise approach for investigation for RAS still remains initial renin estimation followed by a captopril scan for estimating the dependency of glomerular filtration rate (GFR) on A-II and if needed an angiogram combined with angioplasty [12, 14, 18]. In our patient A-II blockade during the first renal scan led to such profound decrease in BP that the child had cardiac ischemia due to hypotension. The BP of 90/60 at that time would be a normal BP for most children of his age but was relatively low for him. Continuation of A-II blockade for treatment of HTN would have led to loss of GFR mostly on the affected side. As our aim has been to preserve the left kidney function it has not been a treatment option.

The toddler also suffered from delay of milestones, failure to thrive and had speech delay at the age of 18 months prior to the diagnosis of HTN. Now 2 years later all of those symptoms have resolved with control of BP. This underlies the importance of measurement of BP and early detection on HTN at any age.
Conclusion:

In summary, in children the combination of hypereninemic malignant HTN with hyponatremia (HHS) does occur and ruling out renal ischemia due to RAS is strongly recommended.
Abbreviations:

hyponatremic hypertensive syndrome (HHS)
hypertension (HTN)
renal artery stenosis (RAS)
angiotensin II (A-II)
blood pressure (BP)
magnetic resonance imaging (MRI)
magnetic resonance angiogram (MRA)
peripheral renin activity (PRA)
intravenous (IV)
left ventricular hypertrophy (LVH)
glomerular filtration rate (GFR)
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References:


**Figure Legend:**

Figure 1. MRA of the left kidney (Patient 1) showing at least two renal arteries with stenosis (black line).

Figure 2. Renal angiogram of the left kidney (Patient 1) with triple renal artery stenosis.

Figure 3. Aorto-renal bypass (Patient 1):

A. Triple (A,B,C) left renal artery stenoses

B. Bifurcated left hypogastric artery autograft harvest

C. A and B renal arteries spatulated and anastomosed

D. Creation of a common renal artery

E. End-end repair of left renal vein

F. End-side anastomosis of the new renal artery and aorta