

Pseudo-Hypo Aldosteronism Type II

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A 50-day-old infant diagnosed as meningitis had persistently elevated serum potassium, low serum bicarbonate and normal serum sodium. She had metabolic acidosis with low TTKG, low serum renin and low normal serum aldosterone with no renal failure or extra renal causes of hyperkalemia. Hence a diagnosis of Type II pseudo-hypoaldosteronism was made. She was started on oral thiazide following which her serum electrolytes normalized.

Key words: Hyperkalemia, Hypertension, TTKG.

Hyperkalemia is one of the electrolyte disturbances noted among children admitted for intensive pediatric care for various conditions. Renal failure is the common cause of hyperkalemia in most of these children. In the absence of renal failure the cause of hyperkalemia should be found out early, as management is not only the treatment of hyperkalemia but also the treatment of the primary condition causing hyperkalemia. Pseudo-hypoaldosteronism (PHA) as a cause of hyperkalemia should be remembered. We describe here an infant presenting with hyperkalemia due to Type II PHA.

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Manuscript received: April 8, 2004;

Initial review completed: July 26, 2004;

Revision accepted: February 8, 2005.

Case Report

A 50-day-old female infant, first born to non-consanguineous parents, delivered by LSCS for non-progression of labor was brought with seizures associated with fever. On examination she was febrile and irritable. She had a B.P. of 90/60 mm of Hg (<95th percentile). Neurological and other systemic examinations were essentially normal. Blood investigation showed a total white cell count of 11,400 cells/cumm with differential count showing neutrophils 18%, lymphocytes 79% and eosinophils 3%. Blood CRP was negative and her CSF showed 35 cells per HPF with neutrophilic predominance. Her CSF sugar was 22 mg/dL with a concomitant blood sugar of 50 mg/dL. Hence, she was treated for meningitis with parenteral ceftriaxone. Her fever subsided with no recurrence of seizures. Incidentally her serum electrolytes showed Na^+ 136mEq/L, K^+ 6.3 mEq/L, Cl^- 112 mEq/L and HCO_3^- of 16 mEq/L. Child had metabolic acidosis by ABG. Her serum creatinine was 0.4 mg/dL. Ultrasonogram of her cranium and abdomen were normal. Her Se.K^+ persistently remained >5.5 mEq/L with low serum bicarbonate and normal serum sodium in spite of being kept on potassium free fluids and potassium elimination measures, even 10 days after admission. In view of the persistently elevated serum potassium even after appropriate corrective measures and in the absence of extrarenal causes of hyperkalemia, child was evaluated for a renal tubular cause. To ascertain the cause of persistently high serum potassium, TTKG (transtubular potassium gradient) was estimated by the formula: $\text{TTKG} = \frac{\text{Urine potassium} \times \text{Serum osmolality}}{\text{S. potassium} \times \text{Urine osmolality}}$. Her biochemistry showed Se.K^+ of 6 mEq/L, S. osmolality of 291 mOsmol/kg, with a concomitant urine potassium of 3.6 mEq/L, creatinine 30 mg/dL, calcium 5 mg/dL and osmolality of 166 mOsmol/kg. Her calculated TTKG was 1.05 ($3.6 \times 291 / 6 \times 166$) against a

normal value of 4-10. This suggested a primary tubular disorder of potassium excretion. On further evaluation, she had low serum renin of 2.15 pg/mL (normal 4-8 pg/mL) and serum aldosterone of 85.4 pg/mL (normal 50-950 pg/mL). Hence in a child with hyperkalemia, metabolic acidosis with normal Se Na^+ , normal blood pressure, low TTKG, low S. renin and low normal S. aldosterone levels, a diagnosis of type II pseudo-hypoaldosteronism (Spitz-Weinstein syndrome/Gordans syndrome) was made. Infant was started on oral thiazide 12.5mg/day in two divided doses. On review after 2 weeks, the infant was found to have gained 500 g and had serum Na 134 mEq/L, serum K^+ 4.6 mEq/L, serum chloride 102 mEq/L and serum bicarbonate of 24 mEq/L.

Discussion

PHA is a disorder of electrolyte homeostasis characterized by an apparent state of renal tubular unresponsiveness to the action of aldosterone and is manifested by salt wasting, hyperkalemia and metabolic acidosis. There are 2 types of PHA namely type I and type II. In Type I PHA, the defect lies in the mineralocorticoid receptors, which are defective in function. The defect can be isolated renal or can involve multiple target organs. Natriuresis is typical of Type I PHA and is absent in Type II PHA. In Type II PHA, the principal defect is increased chloride reabsorption in the distal nephron. Hence it is known as chloride shunt defect. It is also known as, Gordon's syndrome. It is a familial syndrome of arterial hypertension, hyperkalemia, metabolic acidosis, suppressed plasma rennin activity and normal glomerular function and was first described in 1964(1). In 1970, it was described as a new clinical entity by Gordon, *et al.*(2). Approximately 100 cases of the so-called Gordon syndrome have been reported in literature(3). Hypertension is a presenting feature in adolescents and adults. There have been reports in children who present with short stature, hyperkalemia and metabolic acidosis

but with normal blood pressure (Spitz-Weinstein Syndrome)(3-6). It is transmitted by an autosomal dominant trait. Three different loci in chromosomes 1q 31-42, 12p 13.3 and 17p11-q21 were identified. Recently, mutation of WNK1 gene and WNK4 gene has been implicated. WNK1 gene is located in chromosome 12p and it encodes for WNK1 kinase. WNK4 gene is located in chromosome 17p and encodes for WNK4 kinase(7). Basic pathophysiological defect is increased reabsorption of NaCl by distal tubules. WNK1 and WNK4 kinases are localized to the distal nephron segments and play a key role in homeostasis of Na^+ reabsorption and H^+ and K^+ secretion. WNK1 is located in the cytoplasm whereas WNK4 is located in the tight junctions. When mutations of these genes occur, there is an increased transcellular or paracellular chloride conductance in the distal tubule thereby increasing NaCl absorption. This causes firstly a decreased delivery of sodium to the collecting ducts, thereby causing disturbance of the electrical gradient in the tubules and decreased H^+ and K^+ secretion leading to hyperkalemia and metabolic acidosis(8). Secondly, sodium retention causes increased intravascular volume, which causes hypertension and suppression of renin and aldosterone. In children and adults the usual presentation is short stature with arterial hypertension. In infancy laboratory findings of hyperkalemia, hyperchloremic metabolic acidosis, hyporeninemia and hypoaldosteronism with normal GFR may be the only manifestations. Rarely, it may be associated with hypercalciuria and calcium oxalate stones. The whole condition is reversible when there is increased distal delivery of NaCl(9). Furosemide achieves this. But it causes increase in hypercalciuria and thus increasing the chances of urolithiasis. Thus hydrochlor-thiazide (1.5-2.0 mg/kg) is effective in reversing the biochemical changes. It also reduces the net calcium excretion and thus the chances of urolithiasis. Medications have to

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given for life long and its long term prognosis is uncertain.

Conditions with hyperkalemia that have to be excluded in this background include hyporeninemic hypoaldosteronism, type IV RTA, type I RTA with hyperkalemia and isolated potassium secretory defect. On the background of sepsis, hypoaldosteronism of critically ill should also be considered. Major consequence of true hyporeninemic hypoaldosteronism is not salt wasting but rather a condition in which modest to severe hyperkalemia is associated with a modest metabolic acidosis, which indicates abnormalities in the secretion of potassium and protons. This situation is commonly seen in children with interstitial nephritis due to various causes and also in adolescents with diabetic nephropathy. Various drugs like ACEIs and ARBs can lead to hyperkalemia. Type IV renal tubular acidosis with characteristic features of hyperkalemia and metabolic acidosis can occur with or without renal insufficiency. Need for alkali therapy and modalities to reduce serum potassium are diagnostic features in these conditions. Type I RTA with hyperkalemia is characterized by distal RTA with hyperkalemia and need for alkali therapy is important. Isolated potassium secretory defect is relatively rare. The biochemical response to thiazide in Gordon syndrome is peculiar due to the chloride shunt.

To conclude, infants presenting with hyperkalemic metabolic acidosis with normal anion gap, serum sodium and blood pressure with low TTKG, low serum renin and reduced or low serum aldosterone levels can be diagnosed as Spitz Weinstein syndrome and they respond well to thiazide therapy.

Contributors: NP carried out the clinical work. VS was the consultant pediatrician in charge of the child. MVK and BRN supervised the clinical work and drafted the paper along with NP. BRN will act as the guarantor of the paper.

Funding: None.

Competing interests: None stated.

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