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Pseudohypoaldosteronism Secondary to High Output Ileostomy: A Unique Report in an Infant

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Abstract

Salt-losing crisis in an infant should warrant extensive work up. Pseudohypoaldosteronism is a rare condition which is characterized by hyponatremia, hyperkalemia, metabolic acidosis and is associated with high levels of plasma aldosterone. It can be primary or secondary. We report a case of an infant presented with salt-losing crisis and was found to have pseudohypoaldosteronism secondary to excessive losses through ileostomy. This cause of pseudohypoaldosteronism had never been reported previously in children. Additionally, we report an extremely rare association of pseudohypoaldosteronism with thrombocytosis, which can be used as a useful predictor of impending adrenal crisis.

Keywords: Pseudohypoaldosteronism; Secondary; Salt-losing crisis; Ileostomy; Thrombocytosis

Abbreviations:

PHA - Pseudohypoaldosteronism

Introduction

Pseudohypoaldosteronism (PHA) is a rare condition characterized by salt wasting, hyperkalemia and metabolic acidosis associated with high levels of plasma aldosterone. It could be primary or secondary [1,2]. We present the first reported case – to our knowledge- of an infant with secondary pseudohypoaldosteronism due to excessive gastrointestinal losses through ileostomy. Due to significant deficits in sodium and water, aldosterone can no longer facilitate potassium excretion in presence of a profound tubular sodium loss; which would result in hyperkalemia. Additionally, we present the unique association of secondary pseudohypoaldosteronism and thrombocytosis, which to our knowledge, was not reported previously. Thrombocytosis, in this setting, can be used as an important predictor of impending salt-losing crisis.

Case Report

A female infant was born at 35 weeks gestational age with birth weight of 2.6 kg. Antenatally, she was found to have an abdominal mass of unknown origin, so the patient was admitted to neonatal intensive care unit immediately after birth.

Abdominal and pelvic computed tomography scan showed a huge cystic lesion with marginal calcification and compression effect on the intestine. Diagnostic laparotomy was done in the first day of life and showed ileal perforation with meconium cyst formation. Drainage of meconium was done with terminal ileum resection and creation of ileostomy.

	First Episode	Second Episode	Third Episode	Normal Range
Na (mEq/L)	126	131	130	135-145
K (mEq/L)	7	7.8	6.5	3.7-5.9
Aldosterone (ng/dL)	637	>1000	-	7-99
Renin (ng/mL/hr)	5.9	13.3	-	2.4-37
Platelets (k/mm^3)	1080	496	700	150-400
17-hydroxyprogesterone (nmol/L)	8	-	-	< 10
Cortisol (nmol/L)	158	-	-	81.9-957.9
Adrenocorticotropic hormone (pg/mL)	5.8	-	-	5-46

Table 1: Biochemical and hormonal profile of the patient during the recurrent salt-losing crises.

Postoperatively, the patient received total parental nutrition for one week, after which feeding was started gradually and intravenous fluids were discontinued completely within 2 weeks. At one month of age, the infant developed severe dehydration due to excessive losses of gastrointestinal fluids through the ileostomy. She had delayed capillary refill and hypotension. Laboratory testing revealed hyponatremia, hyperkalemia and metabolic acidosis. Blood glucose was normal. Adrenal insufficiency was suspected so hormonal work up was sent and the patient was given hydrocortisone, first as stress dose and then was continued on supraphysiological dose, in addition to sodium

supplement with intravenous fluid. Sodium polystyrene was used to treat hyperkalemia.

Hormonal work up showed picture of pseudohypoaldosteronism (Table 1). So hydrocortisone was tapered down and discontinued. The patient was managed with salt supplement, in addition to adequate hydration. Two days prior to the salt-losing crisis, the patient developed thrombocytosis with platelet count of $1080k/mm^3$ (NL: $150-400k/mm^3$), which returned back to normal with the restoration of normonatremia. There were no clinical or laboratory signs of anemia or sepsis, and cultures were all negative.

One month later, the patient had 2 other episodes of salt-losing crisis, one month apart (Table 1). It was noticed that those episodes coincided persistently with episodes of high output from the ileostomy. After closure of ileostomy, which was done 3 months after the first episode of salt-losing crisis, no further episodes of salt-losing crisis recurred over a follow up period of 6 months. Serum electrolytes, aldosterone level and platelet count, were all normal during this period (Table 2).

	2 days after ileostomy closure	1 week	1 month	4 months	Normal Range
Na (mEq/L)	141	135	135	139	135-145
K (mEq/L)	4.1	4.1	5.3	5.4	3.7-5.9
Aldosterone (ng/dL)	-	-	94.2	-	7-99
Platelets (k/mm³)	348	234	-	-	150-400

Table 2: Serum electrolytes, aldosterone level and platelet count of the patient after closure of ileostomy.

Discussion

Pseudohypoaldosteronism (PHA) is a heterogenous group of disorders, characterized by hyponatremia, hyperkalemia, metabolic acidosis and abnormally elevated plasma aldosterone level. Because of hyponatremia and hyperkalemia, the differential diagnosis should include congenital adrenal hyperplasia, isolated aldosterone synthase deficiency and adrenal insufficiency [1,2].

Pseudohypoaldosteronism has been classified into three distinct types, primary hereditary, namely Type 1 and Type 2, and secondary [3].

Type 1 pseudohypoaldosteronism was first described in a male infant with salt wasting and failure to thrive in the absence of renal or adrenal defect in 1958 [4]. This rare syndrome mainly starts during the neonatal period, either as renal form of autosomal dominant inheritance due to a mutation of the mineralocorticoid receptor gene or a severe systemic form of autosomal recessive inheritance due to a mutation of the epithelial sodium channel (ENaC) gene [5,6]. Type 2 pseudohypoaldosteronism is a rare familial renal tubular defect characterized by hypertension and hyperkalemic metabolic acidosis in the presence of low renin and aldosterone levels. It is linked to loss-of-function mutations in WNK1 or WNK4 genes [7,8].

Secondary causes of pseudohypoaldosteronism include: urinary tract infection, nephropathy, medications and gastrointestinal losses. Systemic lupus erythematosus, sickle cell anemia, acute renal allograft rejection, and chronic allograft nephropathy are among the other causes [9,10]. Most reports of secondary pseudohypoaldesteronesim are for urinary tract infections with renal anomalies. In those patients, there is transient aldosterone resistance in renal tubular cells [10]. Although the mechanism of aldosterone receptor resistance is not well understood, the underlying cause of tubular resistance could be associated with decreased sensitivity of mineralocorticoid receptor due to cytokines like transforming growth factor (TGF)-β and parenchymal scarring secondary to obstruction [11].

Pseudohypoaldosteronism in our patient was secondary to significant gastrointestinal losses through ileostomy. The recurrent salt-losing crises, coincided persistently with episodes of excessive gastrointestinal losses through ileostomy, and the condition resolved when the ileostomy was closed.

Pseudohypoaldosteronism secondary to excessive gastrointestinal losses through ileostomy is under-reported in adult population [12-14], and had never been previously reported in children. Colon and ileum are key sites for sodium and water absorption. Significant defects at these sites will cause depletion of sodium and water, resulting in activation of renin-angiotensin system. The kidney will respond appropriately by decreasing urinary sodium excretion. When sodium and water absorption becomes critically low, aldosterone can no longer facilitate potassium excretion in presence of a profound tubular sodium loss; which would result in hyperkalemia [13,14].

Another unique and extremely important finding in our patient, is the development of thrombocytosis, which preceded salt-losing crisis by two days. The sympathetic nervous system during a salt-losing crisis is activated to maintain vascular tone. Epinephrine reverses the negative effects of hyperkalemia on the heart by lowering serum potassium. At the same time, epinephrine is one of the most important causes of reactive thrombocytosis [15-17]. The association of thrombocytosis with pseudohypoaldosteronism is extremely rare. Only two case reports were published in literature [17,18]. One was for a 6-month-old infant with autosomal recessive pseudohypoaldosteronism [17], who had four hospital admissions over 6 months for salt-losing crises, with each episode she had thrombocytosis which regressed to normal after maintenance of normonatremia with salt supplementation. The other case was for an infant with autosomal dominant pseudohypoaldosteronism type 1 who, in addition, presented with bilateral pneumthoraces at birth [18].

The absence of thrombocytosis except with the occurrence of salt-losing crisis, and the fact that thrombocytosis can occur just before the crisis, indicates that thrombocytosis could be used as a predictor of a salt-losing crisis in patients with pseudohypoaldosteronism.

In conclusion, the case we are presenting is the first reported case - to our knowledge- of pseudohypoaldosteronism secondary to excessive gastrointestinal losses through ileostomy in the pediatric population. This unique cause of such a rare condition should be included in the differential diagnosis for children presented with adrenal crisis and significant gastrointestinal losses; especially in a patient with ileostomy. Additionally, the unique association of thrombocytosis with secondary pseudohypoaldosteronism, can be used as an important predictor of an impending salt-losing crisis.

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