Case Report

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Association of Distal Renal Tubular Acidosis with Hypercalcemia; Report on Three Cases

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Abstract

Background: Hypercalcemia is an endocrine emergency that should be diagnosed as soon as possible and managed carefully. For better management multiple causes of hypercalcemia must be taken into consideration.

Case presentation: We observed three infants with hypercalcemia and distal renal tubular acidosis at the time of diagnosis during 5 years. The patients were referred with severe dehydration and failure to thrive.

Conclusion: There was no reason for hypercalcemia found in these patients except distal renal tubular acidosis. So we suggest distal renal tubular acidosis as a cause for hypercalcemia.

Key Words: Hypercalcemia; Distal renal tubular acidosis; RTA; Failure to thrive

Introduction

Hypercalcemia may be caused by hyperparathyroidism, hyperthyroidism, vitamin D intoxication, malignancy, low phosphate diet, sedentary life style, and William's syndrome[1].

Renal tubular acidosis (RTA) is a kind of hyperchloremic anion gap acidosis. Its pathogenesis is accepted to be a defect in urine acidification. Types of RTA include:
Type I: distal RTA
Type II: proximal RTA
Type IV: mineralocorticoid deficiency

Distal RTA was described in 1949 as a clinical syndrome with hypokalemia. hyperchloremic metabolic acidosis and inability to decrease urinary pH to <5.5, nephrocalcinosis, nephrolithiasis, osteo-malacia and rickets[4]. As the distal part of nephron maintains the pH gradient between urine and blood, the failure to do this, is called distal RTA (dRTA)[5]. In dRTA, there is no evidence of hypercalcemia[1-5].

In 2002, Maruyama reported a 28-day-old newborn with dRTA and hypercalcemia and

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suggested that distal RTA could occur with hypercalcemia only in neonatal period[6]. Pela in 2003 introduced two 5-month-old infants with distal RTA and hypercalcemia, so the association of hypercalcemia and distal RTA in other ages became obvious[7].

In this study we introduce three cases with distal RTA associated with hypercalcemia without any other etiology being found for hypercalcemia.

Case presentation

First patient: A 3-month-old female infant was admitted with recurrent vomiting in 2001. Birth weight 3250 gr. Dehydration, depressed fontanel, dried mucosa and irritability was noted. Laboratory data is reviewed in table 1.

In sonography, there was diffused severe, bilateral Medullary nephrocalcinosis. After rehydration with normal saline, potassium,

Table 1- Clinical and laboratory findings in patients

	First patient	Second patient	Third patient
Age (months)	3	4.5	2
Major clinical manifestation	FTT, recurrent vomiting, dehydration	Recurrent vomiting, lethargy, dehydration, constipation	Poor feeding, lethargy, weight loss
Calcium (mg/dl)	15	12.7	15.6
Phosphate (mg/dl)	5	3.4	6
Bun (mg/dl)	40	14	66
Creatinin (mg/dl)	1.1	0.8	0.6
Sodium (meq/l)	131	135	138
Potassium (meq/l)	2.9	2.2	2.9
Chloride (meq/l)	113	115	119
Total Serum Protein (gr/dl)	5.7	5.5	5.9
Serum pH	7.22	7.29	7.26
Serum Bicarbonate (meq/l)	14.7	10.8	6
Anion gap [Na-(Cl+HCO_3)](meq/l)	7	10	13
Parathyroid hormone	↓	↓	↓
25 (OH) Vit D_3	Nl*	Nl	Nl
Cortisol	Nl	Nl	Nl
Thyroid function test	Nl	Nl	Nl
24 hr urine Ca (mg)	17 (>5 mg/kg/day)	81.9 (10 mg/kg/day)	15 (>4 mg/kg/day)
Maternal Ca (mg/dl)	9.6	10.2	9.6
Urine specific gravity (gr/ml)	1.004	1.005	1.004
Urine acidity (pH)	7.8	7	7

* Normal

chloride and sodium bicarbonate for three days, recovery occurs. Treatment continues with administration of polycitrate. At beginning 5 meq/kg/day bicarbonate was needed and now she needs 2 meq/kg/day. In the meantime the patient is 5 years old and weighs 18.5 kg.

Second patient: A 4.5-month-old female infant whose parents are first degree relatives of the first patient (Mothers are sisters and fathers are brothers). She was admitted in 2001 with recurrent vomiting, lethargy and dehydration. Patient had been well until 20 days before admission and then recurrent vomiting, irritability, confusion and dehydration occurred. Constipation was mentioned during that 20 days. Her weight on admission was 5300 gr (<5%).

Laboratory findings are reviewed in table 1. Sonography showed bilateral Medullary calcification. After treatment with normal saline and sodium bicarbonate for two days, without diuretic or corticosteroid therapy, hypercalcemia and acidosis could be corrected. Now she is 5 years old and weighs 18 kg (50%). Under treatment with 2 meq/kg/day bicarbonate as Shohl's and polycitrate solutions she remains without hypercalcemia.

Third patient: A 2-month-old female infant was admitted in 2002 with poor feeding, lethargy and weight loss after birth. She weighed 3500 gr at birth with good Apgar scores. At admission she was severely dehydrated and weighed 3200 gr (5%). Sonologist reported bilateral Medullaryy nephrocalcinosis. After supportive care and furosemide adminstration (1 mg/kg/day) for 3 days, recovery occurred. The patient is now normocalcemic under treatment with polycitrate solution in outpatient clinic.

Discussion

Symptoms of hypercalcemia include muscle weakness, anorexia, nausea, vomiting, constipation, polyuria, polydipsia, weight loss and fever. In addition, prolonged hypercalcemia causes nephrocalcinosis and progressive deterioration of renal function[2]. These findings commonly were present in our patients.

Insufficiency of urine acidification and need for bicarbonate therapy for 5 years in the first and second patient and occurrence of nephrocalcinosis are the reasons for diagnosis of dRTA. Also laboratory data and bilateral Medullaryy nephrocalcinosis in the third patient are typical for dRTA. The common point in these three patients is the presence of dRTA and transient hypercalcemia without recurrence in early infancy. Also in other studies, the oldest patient was 5 months old[6,7,8].

In a letter published in Pediatric Nephrology, Rodriguez-soriano et al commented that dRTA is a possible etiology of hypercalcemia in newborns[9]. In Maruyama study, hypercalcemia and dRTA was present in a 28-day-old newborn with weight loss and dehydration. Hypercalcemia was corrected after 7 days of fluid and alkali therapy. Seven months later the treatment was discontinued to rule out transient types of dRTA, hypercalcemia with dRTA recurred and this confirmed the association between hypercalcemia and dRTA.

In Pela study two 5-month-old infants are introduced. In both of them hypercalcemia and acidosis was corrected after 2 days of therapy. This study proved that hyper-calcemia and dRTA may occur after neonatal period.

Association of hypercalcemia and distal RTA may be caused by:

1. Severe decrease in extracellular volume at the time of hospital admission (raised BUN). This causes decreased glumerolar filtration rate and consequently increased calcium reabsoption in proximal tubules as seen in thiazide therapy.
2. Acidosis causes bone breakdown and release of calcium from bone. The decreased glumerolar filtration rate and defect in calcium excreation, leads to hypercalcemia.

3. Renal immaturity in early infancy may predispose to hypercalcemia which is not seen is older children.

Conclusion

This study introduces three patients with distal RTA and hypercalcemia. The cause of hypercalcemia could be assumed idiopathic. Distal RTA causes transient hypercalcemia, but under certain circumstances, hypercalcemia can be suggested as a cause of dRTA.

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