A rare cause of hypercalcemia in childhood: hypercalcemia associated with parathormone-related peptide

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Background

Parathormone-related peptide (PTHrP) regulates tissue calcium concentration by acting in paracrine or autocrine ways. It is mostly responsible for paraneoplastic hypercalcemia seen in adults. Paraneoplastic hypercalcemia in children is rarely reported in ALL, medulloblastoma and hepatoblastoma (0.4-0.7%). In experimental studies, PTHrP is shown to be synthesized apart from neoplastic tissue (glomerulus and tubule cells). Hypercalcemia associated with PTHrP in patients with renal dysplasia is rare. We report a case of an infant with renal dysplasia, who presented at 5 months with hypercalcemia, low serum phosphate, suppressed PTH, low 25-hydroxyvitamin D (25-OHD) levels, and high calcitriol and PTHrP levels.

Case Report

- 5-month-old male patient was referred for hypercalcemia.
- He was born on 29th gestational week with a birth weight of 1330 gr, peritoneal dialysis was performed owing to bilateral renal hypoplasia.
- He was on Vitamin D prophylaxis (400 IU/d)
- Thiazide diuretics or other medications which can cause hypercalcemia were never used.

Physical examination;

- Length -3.32 SDS
- Weight -3.80 SDS
- Head circumference: -2.05 SDS
- No sign for subcutaneous fat necrosis or skeletal dysplasia.
- The examination of other systems was normal.

Laboratory evaluation;
Urea: 43 mg/dL (N, 10-38 mg/dL), Creatinine: 3.0 mg/dL (N, 0.4-0.7), Ca:13.7 mg/dL(N, 8.8-10.8), P: 2.2 mg/dl (N, 4-7.0), Mg: 2.5 mg/dL (N, 1.8-2.6), 25 (OH)D3: 97.1 ng/mL (N, 20-100), 1-25 (OH)D3: 60 pmol/L (N, 16.4-81), PTH: 6.64 pg/ml (N, 10-69) pH: 7.38 (N, 7.35-7.45) HCO3:24 mmol/L (N, 22-26). TSH: 3.1 mU/L (N, 0.34-5.6), free T4: 0.9 ng/dL (N, 0.54-1.24), Cortisol (08:00 am) : 9,8 ug/dL (N, 6.7-22.6)
Radiologic evaluation: Skeletal survey was normal.
Echocardiographic evaluation: Normal.

Clinical Follow-up
Primarily, in the etiology PTH independent hypercalcemia was thought with these findings. Vitamin D poisoning or *CYP24A1* mutation were ruled out in the patient with low phosphorus level and normal vitamin D metabolites. Jansen's Metaphyseal Dysplasia was not considered in the patient with no metaphyseal dysplasia or rickets findings in radiologic evaluation. PTHrP level was high 5.9 pmol/L (Normal, <2.0). In bone marrow examination and imaging studies, no evidence for malignancy was established. Due to hypercalcemia which did not respond to hydration and furosemide treatment, pamidronate infusion was applied. Serum calcium level returned to normal after pamidronate and hypercalcemia did not recur in clinical observation.

Table 1. Laboratory findings and its course with treatment

	1st day IV hydration	2nd day IV hydration	4th day IV hydration Furosemide	5th day Pamidronate	6th day	7th day
Calcium (mg/dL) (N, 8.8-10.8)	13.7	14	13.5	13.3	11.2	10.9
Phosphorus (mg/dL) (N, 4.0-7.0)	2.2	2.3	1.7	2	1.5	1.6
ALP (IU/L) (N, 82-383)		1631			1432	
PTH (pg/mL) (N, 10-69)		6.64			5.17	

Conclusion

Although hypercalcemia associated with PTHrP mostly emerge as a paraneoplastic syndrome, it can be rarely seen in renal developmental pathologies. Hypercalcemia associated with PTHrP should be thought in the differential diagnosis of cases followed up with renal hypoplasia/dysplasia and those in whom hypercalcemia has developed in their clinical observation.