

# An Infant with Neonatal Hypoparathyroidism: Case Report

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Parathyroid hormone (PTH) and 1,25-(OH)<sub>2</sub> vitamin D play key roles in the regulation of calcium and phosphate balance. Circulating levels of PTH can change within seconds after an alteration in serum calcium. When the serum calcium falls, PTH is rapidly released and acts quickly to promote calcium reabsorption in the distal tubule and the medullary thick ascending limb of Henle's loop. PTH also stimulates the release of calcium from the rapidly exchangeable pool of bone calcium and a chronic elevation in serum PTH increases renal 1,25-(OH)<sub>2</sub> vitamin D production. The presented patient had convulsions and was brought to the hospital when she was 45 days old. Her calcium level was very low but PTH level was only subnormal so she was diagnosed with hypoparathyroidism. We are reporting the case to emphasise that during the evaluation of calcium balance disorders, the PTH level should not be interpreted alone but together with the calcium, phosphate and alkaline phosphates (ALP) levels.

**KEY WORDS** Neonatal hypoparathyroidism

## Introduction

Approximately 99 % of the total body calcium is found in the skeleton and the teeth. The remaining calcium is in the extracellular fluids in three forms as ionised, protein bound and complexed calcium. The ionised fraction of the serum calcium controls vital cellular functions such as muscle contraction, neuromuscular transmission, and blood clotting.

Parathyroid Hormone (PTH) and 1,25-(OH)<sub>2</sub> vitamin D play key roles in the regulation of calcium and phosphate balance. When the serum calcium falls, PTH is rapidly released and acts quickly to promote calcium reabsorption in the distal tubule and the medullary thick ascending limb of Henle's loop. PTH also stimulates the release of calcium

from a rapidly exchangeable pool of bone calcium. These actions serve to restore serum calcium levels to normal. If kidney function is normal, chronic elevation in serum PTH increases renal 1,25-(OH)<sub>2</sub> Vit D production. This steroid hormone stimulates both calcium and phosphate absorption across the small intestine. The effect requires at least 24 hours to develop fully and begins to restore normal calcium levels. Achievement of eucalcemia then leads to a downward readjustment in the PTH secretory rate. Any increase in 1,25(OH)<sub>2</sub> Vit D serves to inhibit further PTH synthesis.

Circulating levels of PTH can change within seconds after an alteration in serum calcium (1) PTH secretory rates are related to the serum ionised calcium by an inverse sigmoidal relationship. Low ionised calcium concentrations maximally stimulate secretion, while increases in serum calcium suppress the production and release of PTH. PTH secretion is exquisitely sensitive to very small changes in the calcium concentration, which have substantial effects on the rate of hormone synthesis and release. We present a patient whose PTH level

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was subnormal in spite of severe hypocalcemia, so we emphasise that PTH level should not be evaluated alone but together with the serum calcium level.

### Case Report

The baby was born in a hospital, 3800 gr. in weight, at term, after an uneventful pregnancy. The parents were healthy and were not relatives. She was fed with breast milk alone during the first 20 days, and then formula was added. When she was thirty days old, she had the first generalised tonic-clonic afebrile convulsive attack. Convulsions lasting 2-5 minutes recurred three times in the following half an hour. She was brought to a local hospital. Cerebrospinal fluid examination and EEG were normal, serum calcium level was 4,23 mg/dl, phosphate level was 4mg/dl and alkaline phosphatase level was 951 U/L. Therefore she was given i.v. calcium gluconate. When she was 45 days old convulsions recurred and she was brought to our hospital. The patient's weight was 4600 gr. (50 percentile), height was 58 cm (75 percentile) and head circumference was 38 cm (50 percentile). Her physical examination was normal. The laboratory findings are shown in Table 1. Her ionised calcium level was 0,73 mmol/L (normal: 0,8 - 1,2) and albumin level was 4,2 mg/dl, creatinine level was 0,6 mg/dl, vitamin D<sub>3</sub> level was 14 ng/ml (normal : 10-40). QTc in EKG was 0,5. pH was 7,38, HCO<sub>3</sub> was 21, pCO<sub>3</sub> was 46 mmHg, pO<sub>2</sub> was 99 mmHg (in capillary blood). Her mother's calcium, phosphate and alkaline phosphatase levels were normal and vitamin D<sub>3</sub> level was 9 ng/dl (normal:10-40). Vitamin D<sub>3</sub> (1500 U/day) and calcium lactate containing 75 mg/kg/day elementary calcium was started. Calcium /creatinine ratio in

spot urine was higher than the normal range, therefore considering the high risk of nephrocalcinosis a low vitamin D<sub>3</sub> regimen was established (2). At the present time the patient is nine months old and still needs calcium and vitamin D. She is being treated with vitamin D<sub>3</sub> the dose of which is adjusted according to calcium, phosphate and alkaline phosphatase levels in serum, the ratio of calcium/creatinine in urine and renal ultrasonography.

### Discussion

In this patient total calcium level was low, phosphorus level was high, magnesium level was normal and PTH level was at the lowest level of normal (Table 1). If the low calcium level, the high phosphate level and the clinical signs of the patient are considered alone, the findings suggested hypoparathyroidism. Pseudohypoparathyroidism was out of the question because the patient did not have a high PTH level (3). However, the PTH level being within the normal limits might bias the diagnosis of hypoparathyroidism. At that point care must be taken to consider the PTH level together with the serum calcium level. A normal PTH level despite a considerably low calcium level should make one suspect inadequate response of the parathyroid gland i.e. hypoparathyroidism. It is known that serum PTH level may also be normal in cases of primary hypoparathyroidism and hypomagnesemia (Table 2).

Taking the low calcium level and PTH level which is at the lowest limit of normal into consideration this patient was diagnosed as having hypoparathyroidism. The type of hypoparathyroidism was determined by interpreting the clinical and laboratory findings of the patient.

**Table 1.** Laboratory findings of the patient.

Age (months)	Calcium (mg/dl)	P (mg/dl)	ALP (U/L)	Mg (mg/dl)	PTH (ng/ml)	Urine (Ca/Cre)
1.5/12	4.47	8.52	1108	2.17	0.22	1.1
3.5/12	6.88	8.00	720	-	-	0.56
5/12	7.95	7.5	690	2.8	-	0.3
7/12	9.00	6.8	640	-	-	0.4
9/12	9.29	6.7	543	-	-	0.4

**Table 2.** Differential diagnosis in hypocalcemia (1).

	Serum Ca	Serum PO4	PTH	25 (OH)VitD <sub>3</sub>
Hypoparathyroidism		, N	, N*	N
Pseudo Hypoparathyroidism		, N		N
Mg deficiency		N	, N*	N
Secondary** Hyperparathyroidism				

\* May be normal, but inappropriate to level of serum calcium

\*\* Due to vitamin D deficiency, for example; urinary calcium excretion usually less than 50 mg/24h

This case was not accepted as hypoparathyroidism of maternal origin, because maternal calcium, phosphorus and alkaline phosphatase levels were normal (10,2 and 3,9 mg/dl, 297 U/L respectively) (4). Maternal hypercalcemia is a cause of temporary hypoparathyroidism in the newborn. However such a condition was not present in this patient, because the mother was not hypercalcemic and hypocalcemia was persistent in this patient.

Hypomagnesemia is another cause of temporary hypoparathyroidism in the newborn, especially when the mother is diabetic (5). If hypomagnesemia is due to malabsorption, it may be accompanied by hypocalcemia. However hypocalcemia does not have to be a result of magnesium deficiency. Severe hypomagnesemia not only disturbs PTH release but also causes peripheral resistance against the effects of PTH and disturbance in the synthesis of 1,25(OH)<sub>2</sub> VitD<sub>3</sub>. We did not accept hypomagnesemia as the aetiology of hypocalcemia and hypoparathyroidism because this patient's magnesium level was normal.

The hypocalcemia of the infant cannot be explained by the low Vitamin D<sub>3</sub> level of the mother, because in such a condition serum phosphate level would not rise, whereas PTH level would increase in response to hypocalcemia. Besides the infant would develop severe rickets. In our patient the phosphorus level was high and PTH level was low. If this patient were to develop rickets, it would have been a grade III rickets with the severe hypocalcemia that is present and radiological findings would reflect it. The absence of these findings (besides, the alkaline phosphatase level was in the normal range for her age) ruled out the diagnosis of rickets (6).

We could have suspected Di George syndrome which is characterised by thymus and parathyroid aplasia or hypoplasia, cellular immune deficiency, conotruncal cardiac defects, hypertelorism, microgonadism, low-set and dysmorphic ears, short neck and foot abnormalities; but the absence of Di George syndrome stigma and cardiac defects together with a normal thymus imaging drew us away from the diagnosis of Di George syndrome (7,8). Kenny syndrome was also ruled out, because typical findings of Kenny syndrome were not present either(9). The patient was diagnosed to have primary hypoparathyroidism and treated accordingly.

In conclusion it must be stressed that PTH level should be interpreted together with the serum calcium level, and severe hypocalcemia accompanying a normal or borderline PTH level should make one suspect hypoparathyroidism.

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