

A Case of Hypophosphatemic Rickets with the Secondary Hyperparathyroidism

Bariş Sariakçalı, Esmâ Jamaspishvili*, Mehtap Evran, Murat Sert, Tamer Tetiker

Department of Internal Medicine, Division of Endocrinology, Adana, Turkey

*Corresponding author: esmajamaspishvili@gmail.com

Received August 09, 2014; Revised August 25, 2014; Accepted August 28, 2014

Abstract Secondary hyperparathyroidism is an unusual complication of hypophosphatemic rickets during the treatment. As there is growing evidence that a high phosphate diet may induce secondary hyperparathyroidism and even tertiary hyperparathyroidism caused by hyperplasia of the parathyroid glands. Serum calcium, phosphate and also parathyroid hormone should be measured regularly to catch the early diagnosis of secondary hyperparathyroidism during the treatment of hypophosphatemic rickets patients, since this stage is reversible with the arrangement of calcitriol and phosphate. We report a case of secondary hyperparathyroidism due to hypophosphatemic rickets patient, under the treatment of regular calcitriol and oral phosphate related to her serum phosphate levels. She had been treated since her childhood ages for growth retardation and bone deformities. She had, subsequently developed significant hyperparathyroidism during follow up.

Keywords: *hypophosphatemic rickets, secondary hyperparathyroidism, hypophosphatemia, phosphate therapy*

Cite This Article: Bariş Sariakçalı, Esmâ Jamaspishvili, Mehtap Evran, Murat Sert, and Tamer Tetiker, "A Case of Hypophosphatemic Rickets with the Secondary Hyperparathyroidism." *American Journal of Medical Case Reports*, vol. 2, no. 8 (2014): 158-160. doi: 10.12691/ajmcr-2-8-4.

1. Introduction

Hypophosphatemic rickets (HR) or vitamin D-resistant rickets is a group of renal phosphate wasting disorders including X-linked hypophosphatemic rickets (XLH), also called X-linked dominant hypophosphatemic rickets, autosomal dominant hypophosphatemic rickets and autosomal recessive hypophosphatemic rickets. Patients with familial hypophosphatemic rickets (FHR) features but without a family history of rickets, called sporadic hypophosphatemic rickets [1]. They result from defects in renal tubular reabsorption of phosphate, and share similar clinical and biochemical features such as bone deformity, bone pain, short stature, poor dental development, hypophosphatemia, and inappropriately normal serum 1, 25(OH)2D level [2].

Signs of secondary hyperparathyroidism can regularly be detected in treated hypophosphatemic rickets patients. The rise in serum parathyroid hormone (PTH) is dependent on the amount and the duration of oral phosphate supplementation. The pathogenesis of hyperparathyroidism in hypophosphatemic rickets is still unclear. Thus patients under the therapy of vitamin D and phosphate salt often have a depressed 1,25 dihydroxyvitamin D level, with a resultant increase in PTH values. This stage is termed secondary hyperparathyroidism, which is reversible. It has been noted that phosphorus, independent of serum calcium and calcitriol, increases PTH synthesis and secretion by a post-transcriptional mechanism, as a higher phosphate diet

increases the PTH level and induces hyperplasia of the parathyroid glands [3].

2. Case Report

A 27 year old white woman, was diagnosed with vitamin D-resistant rickets (VDRR) in her 4-th years and has been treated with oral phosphate doses three times daily, potassium citrate, Calcitriol and amiloride hydrochlorothiazide. Family history was normal. she had two brothers with normal constitutional parameters. The parents were of normal body constitution. The patient had no complaints, except pain in the lower limbs after a long walk. On examination, she had a short stature (146 cm), frontal bossing of the cranium, bulging of the costochondral junctions (rachitic rosary) and bowing of the lower limbs.

Her bone mineral density (BMD) measured by DEXA was within normal limits (T-score=1, 02). Nephrological evaluation revealed a normal diuresis (1800 ml/24 h, 2600 ml/24 h), normal urine sediment. Ultrasound of her kidneys were normal without nephrocalcinosis. Parathyroid glands ultrasound and scintigraphy did not reveal any pathological findings. Serum potassium and sodium level were normal. The other laboratory parameters are given in Table 1.

For the first visit to our clinic, we stopped oral phosphate and calcitriol, because the serum phosphate and 25(OH)-vitamin D levels in the blood were in the normal range and PTH level was increased. After three months of treatment PTH levels decreased in the blood, but also

reduced serum phosphate level, so we had to continue treatment with phosphate. She continued treatment with oral phosphate doses four times daily, calcitriol and

potassium citrate. Her condition was stable. serum phosphate and calcium levels were normal range, though PTH level increased.

Table 1.

Laboratory findings (normal range)	Before treatment	After Treatment	
		3 month	6 months
Total serum calcium (8.8-10.2 mg/dL)	11.4	10.1	9.7
[Ca ²⁺] (1.1-1.4 mmol/L)	1.27	1.25	1.23
Serum Protein (6.6-8.7 gr/L)	7.5	7.9	7.8
Serum Phosphate (2.7-4.5 mg/dL)	3.4	1.7	2.5
Serum Creatinine (0.6-1 mg/dL)	0.65	0.52	0.43
Blood Urea Nitrogen (5-20 mg/dL)	10	11.424	9.99
PTH (12-88 pg/mL)	276.6	171.4	199
25(OH)-Vitamin D (20-120 ng/mL)	44	72.9	71.3
FGF23 RU/ml (6.8-71.4)	Not measured	Not measured	Not measured
Urine Calcium (0.9-37.9 mg/dL)	8.6	7.7	7.0
Calcium/creatinine clearance ratio	0.3	0.23	0.05
Urine phosphate (40-140 mg/dl)	145.2	2.9	80.7

PTH- Parathyroid hormone; FGF-Fibroblast growth factor.

3. Discussion

In this case, the diagnosis of hypophosphatemic rickets was made based on her clinical and biochemical features. As is well known all the forms of hypophosphatemic rickets have similar clinical features such as failure to walk and bowing of legs in their early childhood), rachitic changes on X-ray, hypophosphatemia, and normal serum calcium (similar to the findings of our case). But, unfortunately, we could not perform genetic analysis. Based on clinical signs, laboratorial and radiological studies we considered hypophosphatemic rickets. Depending on the patient's gender, manifestation age of the disease and detailed family history allowed us that this could be sporadic form of hypophosphatemic rickets. However, treatment and outcome for all forms of the disease are similar. At present, combined therapy of oral phosphate salt and calcitriol is the best therapeutic approach. Vitamin D usage improve the bone lesions, and phosphate salt supplement contributes to better mineralization and growth velocity. Secondary hyperparathyroidism is a potential complication of the treatment of hypophosphatemic rickets, since phosphate treatment is regularly followed by secondary hyperparathyroidism at the post-prandial period. Theoretically, postprandial hyperphosphatemia may act directly on the parathyroid gland or may induce a fall in ionized calcium, and by this induce hyperparathyroidism [4]. In our patient, the post-prandial rise in serum phosphate did not reach the normal range of serum phosphate concentration, furthermore did not reduce the serum concentration of ionized calcium. Moreover there are some cases described in the literature, where apparent secondary hyperparathyroidism has been reported in HR patients who have never received phosphate supplementation [5].

Because, the patient did not have a bone pain and had no history of severe bone disease, we did not try to normalize serum phosphate levels by excess phosphate supplements. We tried to prevent secondary hyperparathyroidism by concomitant treatment with 1,25(OH)2D3 [6]. When a secondary hyperparathyroidism diagnosis had been established, we withdraw phosphate

supplements and increased calcitriol therapy. After that PTH level decreased, but also reduced serum phosphate level. Based on this we had to continue treatment with phosphate. Serum calcium, phosphorus, vit. D and PTH levels were measured regularly.

As mentioned above Hyperparathyroidism is regularly seen in patients treated with phosphate supplements, although circulating serum phosphate levels do not reach the normal range. The pathogenesis of hyperparathyroidism still remains ambiguous. Thus patients under the therapy of vitamin D and phosphate salt often have a depressed 1, 25-dihydroxyvitamin D level, with a resultant increase in PTH values. This stage is termed secondary hyperparathyroidism, which is reversible. This stage is often viewed as a compensatory response to either depressed 1, 25-dihydroxyvitamin D level or relative hypocalcemia. However, it has been noted that depressed renal 1 alpha-hydroxylase activity due to intracellular phosphate retention is a major factor in the direct increase of parathyroid hormone (PTH) secretion in chronic renal insufficiency [7]. Recently have shown that phosphorus, independent of serum calcium and calcitriol, increases PTH synthesis and secretion by a post-transcriptional mechanism, as a higher phosphate diet increases the PTH level and induces hyperplasia of the parathyroid glands [8]. So, in the presence of elevated PTH levels as seen in secondary hyperparathyroidism, high dose oral phosphate salts may further stimulate PTH secretion via multiglandular hyperplasia of the parathyroid glands.

To prevent the occurrence of tertiary hyperparathyroidism in hypophosphatemic rickets patients, early diagnosis of secondary hyperparathyroidism is important. A lower dose supplement of phosphate salt during secondary hyperparathyroidism, a reversible state, is imperative for the success of calcitriol to control further increase in PTH levels [9].

Declaration of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available upon request for review by the Journal Editor.

Author's Contribution

EJ review of literature and drafted the manuscript; BS have managed the case clinically, participated in the endocrinological treatment, and collected the data; ME collected all medical reports of the patients and performed ultrasound examination; TT participated in the endocrinological treatment and designed the manuscript ; MS contributed the concept of research paper, revised the manuscript critically for important intellectual content and gave final approval of the version to be published. All authors read and approved the final manuscript.

References

- [1] Durmaz E, Zou M, et al. (2012) Novel and de novo PHEX mutations in patients with hypophosphatemic rickets. *Bone* 52 (2013) 286-291.
- [2] Amatschek S, Haller M, Oberbauer R. Renal phosphate handling in human—what can we learn from hereditary hypophosphataemias? *Eur J Clin Invest* 2010; 40: 552-60.
- [3] Slatopolsky E, Finch J, Denda M, et al. Phosphorus restriction prevents parathyroid gland growth. High phosphorus directly stimulates PTH secretion in vitro. *J Clin invest* 97: 2534-2540, 1996.
- [4] Brown EM (2000) Calcium receptor and regulation of parathyroid hormone secretion. *Rev Endocr Metab Disord* 1:307-315.
- [5] Knudtzon J, Halse J, Monn E, Nesland A, Nordal KP, Paus P, Seip M, Sund S, Sodal G (1995) Autonomous hyperparathyroidism in X-linked hypophosphataemia. *Clin Endocrinol (Oxf)* 42:199-203.
- [6] Latta K, Hisano S, Chan JC (1993) Therapeutics of X-linked hypophosphatemic rickets. *Pediatr Nephrol* 7: 744-748.
- [7] Rivkees SA, el-Hajj-Fuleihan G, Brown EM, Crawford JD (1992) Tertiary hyperparathyroidism during high phosphate therapy of familial hypophosphatemic rickets. *J Clin Endocrinol Metab* 75: 1514-1518.
- [8] Alon US, Monzavi R, Lilien M, Rasoulpour M, Geffner ME, Yadin O (2003) Hypertension in hypophosphatemic rickets— role of secondary hyperparathyroidism. *Pediatr Nephrol* 18:155-158.
- [9] Claus Peter Schmitt · Otto Mehls (2004). The enigma of hyperparathyroidism in hypophosphatemic rickets, *Pediatr Nephrol* (2004) 19:473-477.