Case Report
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ALTERNATE DAYS TREATMENT WITH TERIPARATIDE IN POSTSURGICAL HYPOPARATHYROIDISM

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Abstract

The conventional treatment of hypoparathyroidism consists of vitamin D analogues in combination with oral calcium supplementation. This treatment modalities induce chronic hypercalciuria which leads to nephrocalcinosis, nephrolithiasis and renal insufficiency. Here we report the case of a 32-year-old woman who developed hypocalcemia and hypercalciuria under treatment with high doses of vitamin D analogs and oral calcium. She had cerebral calcification, nephrocalcinosis under this treatment. Stable calcium levels were achieved with synthetic human parathyroid hormone treatment that was given in alternate days. PTH appears to be an alternative and effective treatment in hypoparathyroidism.

Key words: hypocalcemia, hypoparathyroidism, synthetic human parathyroid hormone.

INTRODUCTION

Hypoparathyroidism is a hormone deficiency which leads to abnormalities in mineral metabolism that includes hypocalcemia, hyperphosphatemia, and hypomagnesemia. Surgical removal or injury of the parathyroid glands are the most common causes of hypoparathyroidism. This disorder is mostly treated with vitamin D analogs and oral calcium supplementation (1). Chronic hypocalcemia itself and the current treatment modalities may cause some complications.

Chronic hypocalcemia may cause cerebral calcification and visual impairment due to cataracts. Excessive hypercalciuria which leads to nephrocalcinosis, nephrolithiasis and renal insufficiency accompanies the conventional therapy with vitamin D analogs (2). Synthetic human PTH 1-34 is a new treatment option and reduces the urine calcium excretion in hypoparathyroidism and normalizes the serum calcium levels. Here we describe a case with post-surgical hypoparathyroidism with severe hypocalcemia which could not be controlled with vitamin D analogs and

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oral calcium treatment. The patient was successfully treated with alternate days treatment regime of synthetic human PTH.

CASE REPORT

A 32-year-old woman was admitted to our hospital because of tetany and muscle spasms. Thyroidectomy was performed 9 years ago due to multinodular goiter. Although she had high dose oral supplementation of calcium carbonate, magnesium citrate and calcitriol (10 g/d, 1830 mg/d, 5 mcg/d respectively) she had symptoms of hypocalcemia for a long time. On admission the calcium level was 6.4 mg/dL (normal range:8.9-10.3), ionized calcium level 3 mg/dL (normal range: 4.2-5.2), albumin level 3.6 g/dL (normal range: 3.5-5), PTH level 1.4 pg/mL (normal range: 12-72), magnesium level 1.7 mg/dL (normal range: 1.6-2.6), phosphorus level 5.6 mg/dL (normal range: 2.3-4.7), 25 OH D vitamin level 29 ng/ dL (Table 1). She had nephrocalcinosis, bilateral cortical cataracts, and bilateral calcifications in frontal brain parenchyma (Figs. 1 and 2). She had serious gastrointestinal symptoms due to high dose calcium citrate and calcitriol treatment. A 24-h urinary calcium was 175 mg/d (normal range: 100-300), phosphorus 549 mg/d (normal range: 800-1300). Intravenous calcium treatment was initiated (360-630 mg/d intravenous ionized calcium according to the calcium levels and symptoms) to ameliorate her symptoms. Serum calcium levels remained very low, a thiazide diuretic (50 mg hydrochlorothiazide, twice daily) was added to her treatment but she still had symptomatic hypocalcemia(maximum level we achieved was 7.9 mg/dL). After one week we initiated treatment with teriparatide (rhPTH [1-34]) as a replacement for her hypo-parathyroidism. Initial dose was 20 mcg /per day teriparatide (0.4 μ/kg per day with once-daily protocol, her weight was 50 kg, height 163 cm and BMI 18.8 kg/m^2) with 100 mg hydrochlorothiazide, 2 g of oral calcium carbonate, and 1 mcg calcitriol (reducing day by day). After two weeks, because of hypercalcemia (11 mg/dL) rhPTH treatment was switched to alternate days. Stable normal level of serum calcium was achieved within 4 weeks. Calcitriol, calcium supplementation was tappered (calcitriol 0.5 mcg, 1g calcium carbonate) after the onset of PTH administration. 24-h urine calcium excretion was reduced 152 mg/day. After 3 months of treatment serum calcium level was stable, the therapy was well tolerated (Table 1).

DISCUSSION

The conventional treatment of hypoparathyroidism consists of vitamin D analogs in combination with oral calcium supplementation. Treatment with vitamin D analogs causes a tendency toward hypercalciuria. Hypercalciuria increases the risk of renal complications such as nephrocalcinosis, nephrolithiasis, and renal impairment. Hormone replacement therapy with synthetic PTH

Table 1. Biochemical data of the patient with hypoparathyroidism

Analysis	Normal range	Admission	1st week PTH therapy 10μg/day/once daily	4th week PTH therapy 10μg/ alternate day	3rd month PTH therapy 10μg/alternate day
Calcium	8.9-10.3 mg/dL	6.4	11	10.1	9
Phosphorus	2.3-4.7 mg/dL	5.6	-	4	3.5
PTH	12-72 pg/mL	1.4	-	-	-
24-h urine calcium	100-300 mg/d	175	-		152

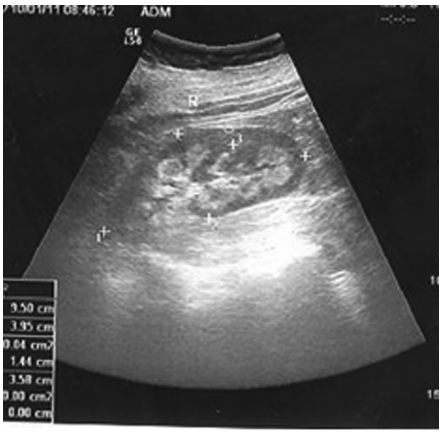

Figure 1. Ultrasound imaging shows nephrocalcinosis.

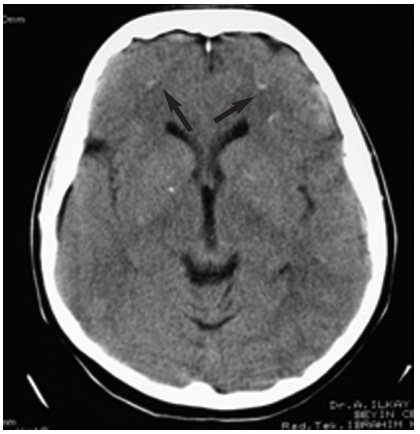

Figure 2. Computed tomography (CT) of the cranium shows microcalcifications in subcortical frontal brain parenchyma.

in hypoparathroidism is another option. Synthetic PTH is mostly used in postmenopausal osteoporosis. Domingo *et al.* described a 53-year old female patient who presented with hypocalcemia after thyroidectomy. Calcitriol, oral calcium and magnesium treatment was unsuccessful. They even could not achieve stable calcium levels with subcutaneous injections of recombinant human PTH (rhPTH). After the rejection of a heterologous parathyroid transplant multiple sc infusions of rhPTH treatment were initiated. Complete normalization of serum calcium was achieved (3). Angelopoulos *et al.* reported a case of idiopathic hypoparathyroidism treated with calcitriol and calcium supplementation for 20 years who subsequently presented with marked hypercalciuria and bilateral nephrolithiasis. Synthetic PTH treatment was successful and normal serum calcium was achieved within 3 weeks of therapy (2). Winer *et al.* showed that once daily treatment of PTH 1-34 maintained serum calcium

levels within normal range and decreased urine calcium excretion compared with calcitriol treatment (4). In another trial, they showed that twice-daily PTH reduce total daily PTH dose provided, reduced bone turnover markers and decreased incidence of bone pain compared with a once-daily regimen (5). In 2002, Winer *et al.* reported the results of a 3-year randomized trial which established the long-term efficacy of twice daily PTH treatment. There was no change in bone and in bone mineral density, despite mild elevation of bone turnover markers comparing PTH to calcitriol and calcium therapy. They showed that PTH(1-34) normalized mean 24-h urine calcium excretion but this did not cause an improvement in renal functions. There were no skeletal malignancies in protocol patients. The study concluded that PTH(1-34) is an effective and safe long-term hormonal replacement therapy for patients with hypoparathyroidism of various etiologies (6). Mahajan *et al.* also described a case of hypoparathyroidism after subtotal parathyroidectomy following renal transplantation which was treated successfully with teriparatide (7).

Our patient suffered from hypocalcemia episodes after thyroidectomy in spite of high doses oral supplementation of calcium carbonate, magnesium citrate and calcitriol treatment. Calcitriol requirement of such high doses is unusual in patients with hypoparathyroidism. Initial recommended dose of synthetic PTH is between 0.4-0.7 mcg/kg per day (2, 5, 6). We preferred once-daily regimen (0.4 μ/kg per day), but our patient had hypercalcemia so we modified the treatment and gave it on alternate days. Winer *et al.* showed that once-daily protocol induced significantly more hypercalcemia than twice-daily protocol (4). Synthetic PTH on alternate days normalized the serum calcium levels in our case. Alternate days PTH, instead of daily or twice daily PTH could be considered as another treatment option. This treatment method will also reduce the cost.

It has been found that long-term treatment of rats with PTH(1-34) caused the unexpected finding of focal bone proliferative lesions, including osteosarcoma (8). The potential development of osteosarcoma, the high cost of synthetic PTH, the inconvenience of injection treatment are the disadvantages of PTH treatment that should be taken into account.

In conclusion, although calcium and vitamin D treatment is cheaper and effective in most of the cases, PTH appears to be an alternative and effective treatment in patients with hypoparathyroidism who do not respond to the conventional treatment. Further study is needed to understand the safety, cost-effectiveness and long-term effects of PTH(1-34) treatment.

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.

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