CASE REPORT

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Use of Recombinant Human Parathyroid Hormone to Treat Hungry Bone Syndrome in Hemodialysis Patient

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ABSTRACT

We report the case of a 35-year-old female with end-stage renal disease on hemodialysis for nine years. She was diagnosed with secondary hyperparathyroidism complicated with a brown tumor in the mandible. After medical therapy failed, she underwent total parathyroidectomy (PTX), which was complicated by severe and prolonged hypocalcemia (hungry bone syndrome). Post-surgery, she required prolonged and frequent intravenous calcium and a high dose of vitamin D resulting in frequent admission with symptomatic hypocalcemia. Her serum magnesium was noted to be in the normal range. She continued to be hypocalcemic for nearly eight months post-surgery despite the intensive treatment. Recombinant human parathyroid hormone (teriparatide) 20 mg daily resulted in normalization of calcium within two weeks. The use of parathyroid hormone proved to be an effective treatment approach in this case. Proper pre-operative preparation and subtotal PTX with an adequate dose of vitamin D and calcium supplement may have been a rational option for this case.

Secondary hyperparathyroidism (SHPT) is a frequently encountered problem in the management of patients with end-stage renal disease (ESRD) on regular hemodialysis. It has been associated with poor patient outcome including accelerated atherosclerosis and metabolic bone disease.[1–3]

Parathyroidectomy (PTX) in ESRD is an effective method after failing medical therapy for normalization of metabolic bone disease.[4] Hungry bone syndrome (HBS) is defined as prolonged and severe hypocalcemia after PTX.[4] The clinical presentation of HBS is related to hypocalcemia ranging from muscle cramps, numbness, tingling sensation, neuromuscular irritability, tetany, and in severe form can lead to a seizure.

The diagnosis of HBS is done by serial measurements of serum calcium level. The treatment of HBS includes oral and intravenous calcium and vitamin D.[4] We report a case of severe and prolonged hypocalcemia post-PTX that did not respond to standard therapy but responded to recombinant parathyroid hormone (PTH) therapy.

CASE REPORT

Our patient was a 35-year-old female with ESRD due to systemic lupus erythematosus on hemodialysis for nine years. She was diagnosed with SHPT complicated with a brown tumor in the mandible. She was treated with a high dose of vitamin D3 and cinacalcet 90 mg with the following laboratory results: PTH = 228.6 pmol/L (1.6–6.9), calcium = 2.1 mmol/L, phosphorous = 1.8 mmol/L, and alkaline phosphatase = 373 IU/L. Nuclear sestamibi scanning showed increased uptake at the parathyroid area (indicating hyperplasia of four parathyroid glands). After the failure of medical therapy for 18 months, she underwent total PTX, which was complicated by severe hypocalcemia an HBS. Post-surgery, she required prolonged and frequent intravenous calcium and a high dose of vitamin D resulting in frequent admission with symptomatic hypocalcemia (serum calcium level < 1.6). Despite the intensive treatment, she continued to be hypocalcemic for nearly eight months post-surgery. At this stage, her compliance to the oral home calcium supplements was questioned. Recombinant human teriparatide 20 mg given daily for seven

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Table 1: Calcium, parathyroid hormone (PTH), phosphorous, and alkaline phosphatase levels in our patient pre- and post-therapy.

Therapy	Calcium level, mmol/L	PTH, pmol/L	Phosphorous, mmol/L	Alkaline phosphatase, IU/L
Pre-PTX, Brown tumor	2.1	228.6	1.8	373
Post-PTX	2.2	1.9	1.8	60
Post-teriparatide therapy	2.0	1.0	0.8	39

PTX: parathyroidectomy.

days followed by three times per week post dialysis, resulted in complete resolution of her symptoms and serum calcium to normalize to 2.2 mmol/L, PTH = 1.9 pmol/L, and alkaline phosphatase = 60 IU/L along with complete regression of the brown tumor [Table 1]. The total duration of therapy with teriparatide was four weeks, after that she was maintained on oral calcium supplements (600 mg eight hourly daily) and vitamin D parenteral during dialysis.

The brown tumor resolved completely post-PTX, and her calcium levels stabilized through the use of teriparatide. There was no resurgence of the brown tumor throughout the observation period of 18 months post-PTX and 15 months post use of teriparatide.

DISCUSSION

HBS is a relatively uncommon complication of PTX for severe SHPT associated with high pre-operative bone turnover. It is clinically evident by rapid, profound symptomatic hypocalcemia associated with hypophosphatemia, hypomagnesemia, and suppressed PTH levels. Hypocalcemia will be prolonged and takes weeks to normalize. The duration of HBS is the time taken to remineralize the skeleton, which is also mirrored by normalization of bone turnover markers.[4]

Data on the prevalence of HBS are scarce and conflicting after the original publication in 1980 of a large case series suggesting that the syndrome develops post-operatively in up to 13% of patients with SHPT.[5–8]

Older age at the time of surgery is a high-risk factor for HBS.[9] Patients who developed HBS have higher pre-operative levels of serum calcium and almost two-fold increased levels of PTH, calcium phosphatase[10,11] and radiological bone disease before surgery.[12]

The treatment aims to replenish the serum calcium deficit by using high dose calcium supplemented with a high dose of the active metabolite of vitamin D.[13] Adequate correction of magnesium deficiency and normalization of bone turnover are required for resolution of the hypocalcemia, which may last several months after successful surgery.

Pre-operative treatment with calcium, active vitamin D, and calcimimetics has been suggested to reduce postoperative hypocalcemia,[14,15] but there is no prospective study addressing this issue. Despite vitamin D and calcium supplementation, our patient continued to have persistent hypocalcemia with frequent admissions. Her serum magnesium remained within the range of 0.9 mmol/L to 1.1 mmol/L throughout the follow-up period. Hence, she was never given a magnesium supplement.

A research group in the US has performed a limited number of studies using recombinant PTH treatment. In their study, once-daily injection with PTH was compared with conventional therapy showing that normocalcemia can be maintained by PTH therapy.[16–18] However, as PTH has a relatively short half-life of 5–10 minutes, another high dose is needed to maintain normocalcemia throughout the day. No report was found on the use in patients with renal disease. In our case, after the use of PTH, serum calcium normalized in two weeks. The patient was asymptomatic and required no further admissions.

CONCLUSION

The efficacy of total PTX was satisfactory with rapid normalization of PTH and resolution of the brown tumor but complicated with severe and prolonged hypocalcemia. The use of recombinant PTH proved to be an effective treatment approach. Proper pre-operative preparation and subtotal PTX with an adequate dose of vitamin D and calcium supplement may have been a rational option for this case.

Disclosure

The authors declared no conflict of interest.

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