CASE REPORT

Persistent hypocalcemia and hungry bone syndrome after parathyroidectomy and renal transplantation in a patient with end-stage renal disease

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ABSTRACT

Hungry bone syndrome (HBS) defines as persistent and severe hypocalcemia after parathyroidectomy surgery. It is treated by oral or venous discrimination of calcium carbonate. The present treatment is mostly effective. Hereby, we describe a 60-year-old man who had developed hyperparathyroidism secondary to end-stage renal disease and then parathyroidectomy was performed for him twice before renal transplantation. Up to 500 vials of calcium gluconate (100 mg/ml calcium gluconate 10%) were administered for him to control serum calcium level after parathyroidectomy and renal transplantation. Furthermore, high-dose calcium carbonate was administered for his outpatient care. Therefore, HBS, which was resistant to standard treatment, was detected for him.

Key words: End-stage renal disease, hungry bone syndrome, parathyroidectomy

INTRODUCTION

Hungry bone syndrome (HBS), defined as prolonged and severe hypocalcemia, is a complication of parathyroidectomy.[1] HBS presents with symptoms of hypocalcemia such as tetany, seizures, numbness and tingling sensations in the fingers and toes, muscle cramps, weakness, and headaches. Diagnosis of HBS is done by serial measurement of serum calcium level. Parathyroidectomy is done because of secondary hyperparathyroidism in patients who are unresponsive to intensive regimen of calcium carbonate, this can be a reason of HBS.[2] The treatment of HBS includes oral and intravenous calcium.[3,4] Here, we report a case of severe hypocalcemia due to postsurgical hypoparathyroidism, and HBS associated with end-stage renal disease (ESRD), which did not response to standard treatment.

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CASE REPORT

A 60-year-old man with symptomatic prolonged hypocalcemia after renal transplantation was presented to Tabriz University of Medical Sciences (Tabriz, Iran), the clinic of nephrology. Family history of hypocalcemia or other metabolic disease was not detected for him. Medical history taking revealed that he was a case of ESRD and had undergone hemodialysis two times weekly since 6 years ago. Parathyroidectomy was done for him as the last step of hyperparathyroidism management, with technique of limited exploration, maintaining one of the parathyroid glands, 3 years ago. Although parathyroid scan with Tc-99m-MIBI had only showed left inferior parathyroid adenoma, abnormal enlargement

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of the left superior and right inferior glands during the surgery had made the surgeon to extract all three glands, mentioned above. The left inferior parathyroid gland was 3.5 g and 2.5 cm × 2 cm × 1 cm. The left superior parathyroid gland was 0.6 g, and the right inferior parathyroid gland was 1 g. Pathologist had reported parathyroid adenoma for the left inferior parathyroid and unremarkable parathyroid glands for two others. The serum total and ionized calcium level were 7.4 mg/dl and 0.88 mmol/L, respectively. He had not showed any symptom of hypocalcemia. He had received calcium carbonate with daily dose of 1500 mg and five vials of calcium gluconate in 500 cc DW 5% serum twice daily. He had discharged with order of using 1500 mg calcium carbonate and 9 capsules of rocaltrol daily. Hemodialysis was done for him during 3 years after parathyroidectomy, twice weekly. Drug history of the patient included the mentioned drugs. Three years after parathyroidectomy, he was being prepared for renal transplant when high level of parathyroid hormone (PTH) was detected for him, so remained parathyroid gland was surgically removed. Calcium levels in this step were similar to the previous hospitalization. He had used six tablets of calcium carbonate daily with total dose of 3000 mg, for 1 month, since the last parathyroidectomy until renal transplantation. In this period, complete survey including cardiac function assessments and endoscopic assessments of the gastrointestinal tract showed appropriate condition of the patient for transplantation. Then, renal transplantation from a stranger healthy donor, with isogroup blood type and also negative crossmatch, was performed for him. Transplanted kidney was placed upside down in the right side, by end-to-side anastomosing renal artery to the external iliac artery, and renal vein to iliac vein. Transplantation was done without any complication. After transplantation, his serum and ionized calcium level was serially checked every day at the same laboratory of Tabriz University of Medical Sciences. The serum total and ionized calcium levels were low, respectively, about 5.8 mg/dl and 0.7 mmol/L in serial measurements. Despite receiving nearly up to 300 vials of calcium gluconate during 25 days of hospitalization, the level of total serum calcium was 7.6 mg/dl and ionized calcium was 0.8 mmol/L while discharging. The mentioned levels of calcium caused no signs and symptoms. The serum phosphorus level was 2.1 mg/dl. Ten days after discharging, he was admitted in the nephrology ward with tingling of the fingers and toes. Laboratory evaluation showed total serum calcium = 7 and ionized calcium = 0.9. Other laboratory findings include: Serum phosphorus = 2 mg/dl, mg = 2 mg/dl, 25-dihydroxyvitamin D (25(OH) D3) = 13.1, PTH = 19.2 pg/ml, alkaline phosphatase = 433 IU/L, lactate dehydrogenase = 1138 IU/L, and urine calcium in 24 h specimen = 100 mg. Bone densitometry of the left hip 2 months after transplantation showed T-score - 3.4 and Z-score - 1.8 which indicated osteopenia. The present hospitalization took more than 2 months, in which the patient was treated by daily infusion of calcium gluconate, oral calcium carbonate, and rocaltrol. Up to 200 vials of calcium gluconate (100 mg/ml calcium gluconate 10%) were administered for this patient and finally the patient's calcium level reached normal range (total serum calcium = 8.9 and ionized calcium = 1.17). Figures 1 and 2 report serial serum ionized calcium and serum total calcium. This patient was discharged with prescription of incoming drugs: 6 tablets of calcium carbonate daily, 12 capsules of rocaltrol daily, a tablet of folic acid daily, a pearl of Vitamin B complex, and immunosuppressive drugs (cyclosporine and prednisolone).

DISCUSSION

Secondary hyperparathyroidism is a high bone turn over state, in which bone formation and resorption are both increased because of increased PTH. Secondary hyperparathyroidism develops in nearly all patients with ESRD.[5] Serum calcium level is regulated by kidneys, bone turn over, and parathyroid glands. Considering mechanisms of secondary hyperparathyroidism, including decreased 1, 25(OH) D levels, hypocalcemia, and hyperphosphatemia, guides the medical management. Phosphate binders, active Vitamin D analogs, and calcimimetics are bases of the treatment of secondary hyperparathyroidism.[6,7] In patients with failed medical treatment, parathyroidectomy is an efficient and safe option.[6] The range of parathyroidectomy due to severe hyperparathyroidism in patients with ESRD ranges from 2.6% to 40%. HBS is a common complication, happening immediately after parathyroidectomy.[8] Furthermore, due to renal insufficiency and bone damage after long-term dialysis, bone disease in patients with renal transplantation is much more than nonrenal transplantation. HBS clinically presents with prolonged hypocalcemia and tetany, tingling of fingers and toes, and other clinical manifestations of hypocalcemia after surgical parathyroidectomy among patients who had increased bone resorption preoperatively. Risk factors for

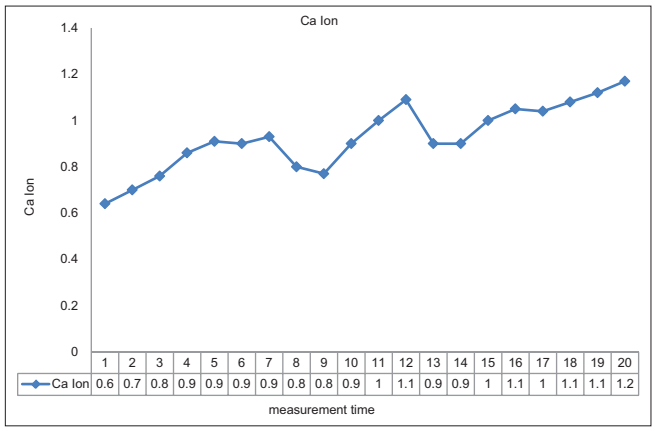

Figure 1: Serial serum ionized calcium was reported every three days

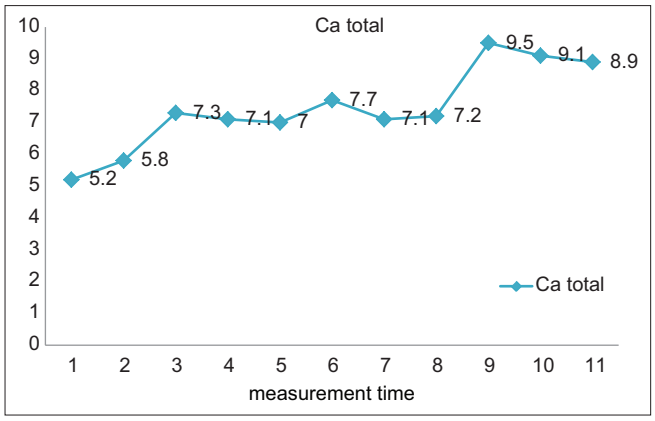

Figure 2: Serial serum total calcium was reported every five days

developing HBS include increased alkaline phosphatase, elevated osteoclastic activity related to osteitis fibrosa, older age, and the volume of parathyroid glands at the time of resection.[1] HBS in transplant recipients is based on preexisting damage to the bone acquired during the renal insufficiency period, damage to the bone starting in the period of transplantation, and modulating influences independent of renal disease or renal transplantation.[9] The present patient with ESRD and secondary hyperparathyroidism had undergone parathyroidectomy and renal transplantation, so high risk of developing HBS was predictable for him. He had very low level of total and ionized serum calcium (respectively, about 7 mg/dl and 0.8–1 mmol/L) although taking abundant oral and intravenous calcium (3 g of elemental calcium) combined with Vitamin D in form of rocaltrol capsule (12 capsules daily). Searching "HBS resistant to treatment" exposed one case report similar to presenting patient, in which the patient had achieved normal calcium levels after 3 months of the consecutive treatment with calcium carbonate.[10] The rare event in this patient is presenting osteopenia, hypocalcemia, and normal level of calcium in urinary output, despite high level of intravenous calcium administration. Working up for the result of this event revealed parenchymal dysfunction of transplanted kidney. This dysfunction may cause the imbalance of calcium level. We believe that the present patient's condition is consistent with HBS in addition to transplanted kidney dysfunction. Resistance to the treatment of hypocalcemia is due to parenchymal dysfunction of transplanted kidney, in our opinion. Hence, when the clinicians face prolonged hypocalcemia in patients with chronic renal dysfunction and parathyroidectomy, they should work up for HBS and consider that long-term treatment may be needed.

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Conflicts of interest
There are no conflicts of interest.

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