Case report

Use of denosumab in parathyroid carcinoma with refractory hypercalcemia

C.V. TONG1, Z. HUSSEIN1, N. MOHD NOOR1, M. MOHAMAD1 and W.F. NG1

From the1 Department of Medicine, Endocrine Unit, Hospital Putrajaya, Pusat Pentadbiran Kerajaan Persekutuan, Presint 7, 62250 Putrajaya, Malaysia

Address correspondence to C.V. Tong, Department of Medicine, Endocrine Unit, Hospital Putrajaya, Pusat Pentadbiran Kerajaan Persekutuan, Presint 7, 62250 Putrajaya, Malaysia. email: tchinvoon@yahoo.com

Learning Point for Physicians

This case illustrates the difficulties in treating hypercalcemia caused by parathyroid carcinoma. However, there are various choices of treatment and in recalcitrant cases, denosumab should be considered as a therapeutic option. It is important to know the vitamin D status of the patient and to monitor for hypocalcemia post treatment.

Use of denosumab in parathyroid carcinoma with refractory hypercalcemia

Parathyroid carcinoma is rare; accounting for ~1% of all the causes of primary hyperparathyroidism.1 When the tumor is no longer amenable for surgery, medical therapy to control the hypercalcemia becomes the main focus of management. Unfortunately, parathyroid carcinoma mediated hypercalcemia is often severe and more resistant to medical therapy. We report a case of parathyroid carcinoma with refractory hypercalcemia treated with denosumab.

A 26-year-old lady with recurrent parathyroid carcinoma initially presented in April 2012 with symptoms of hypercalcemia, a serum calcium of 4.0 mmol/l with intact parathyroid hormone (iPTH) of 176 pmol/l. There was no family history of calcium or parathyroid disorders. She had no hoarseness of voice or palpable neck swelling. Neck ultrasound localized an enlarged right parathyroid nodule measuring 1.5 × 1.6 × 2.4 cm. She underwent right superior parathyroidectomy in May 2012 and the histopathology diagnosis was parathyroid neoplasm of uncertain malignant potential.

She was lost to follow-up and resurfaced a year later with symptomatic hypercalcemia associated with neck pain and significant weight loss. Computed tomography (CT) scan of neck and thorax showed multiple cervical lymph nodes bilaterally. She underwent right hemithyroidectomy and right modified radical neck dissection following this but remained persistently hypercalcemic after surgery.

Four months later a repeat CT scan showed evidence of an aggressive, recurrent disease with multiple matted cervical lymph nodes at the right thyroid bed and right supraclavicular lymphadenopathy. She underwent her third surgery (bilateral neck exploration, completion thyroidectomy, left parathyroidectomy, left neck dissection and resection of local recurrence). Despite this, her calcium levels remained elevated. Histopathology examinations from the last two surgeries were consistent with parathyroid carcinoma with lymph nodes metastases.

As her disease progressed, she required multiple admissions for hypercalcemic crises and developed various complications from severe hyperparathyroidism such as nephrocalcinosis, renal tubular acidosis,
osteoporosis, depression, episodes of acute pancreatitis and cardiac arrhythmias. Hypercalcemia was resistant to standard medical therapy. This comprised of aggressive saline rehydration and intravenous biphosphonate at more frequent intervals, eventually on a monthly basis. She also underwent acute hemodialysis which lowered calcium levels temporarily. Subcutaneous calcitonin was also administered on a few occasions but also did not normalize her calcium levels. Oral cinacalcet was then initiated and titrated to 90 mg thrice daily within 3 months without much response.

Subcutaneous denosumab of 120 mg was given on 1 April 2014 and calcium levels rapidly normalized by the third day and continued to drop further with symptomatic hypocalcemia by day 7 requiring calcium supplements (Figure 1). This was also caused by severe vitamin D deficiency, serum total 25—hydroxyvitamin D was 9.23 nmol/l. She was given oral cholecalciferol at 5000 units per day. She has not required any IV biphosphonate 6 weeks post-denosumab.

Denosumab, a monoclonal antibody that inhibits osteoclast activity has been approved for treatment of postmenopausal osteoporosis and also for prevention of skeletal related events in malignancies with bone metastases. Hypocalcemia has been observed as one of the side effects of denosumab in many trials, presumably due to reduced osteoclast function. In a randomized double blind study comparing denosumab and zoledronic acid for delaying or preventing skeletal related events in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma, 5.7% of patients who received denosumab required intravenous calcium infusions compared to 2.7% in the zoledronic acid arm. With this observation, denosumab has been used in humoral hypercalcemia of malignancy. Vellangi et al. reported that the use of denosumab in their patient with parathyroid carcinoma was able to reduce the need for biphosphonate therapy and admissions for hypercalcemia.

Denosumab is a therapeutic option that can be considered in refractory hypercalcemia of parathyroid carcinoma which is not amenable to surgery. However, careful monitoring of calcium levels post therapy is essential particularly if the patient is Vitamin D deficient to avoid complications from hypocalcemia.

Conflict of interest: None declared.

References