Denosumab for management of refractory hypercalcaemia in recurrent parathyroid carcinoma

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We read with interest the report by Karuppiah et al. (1) on the use of high-dose denosumab for the treatment of refractory hypercalcaemia secondary to parathyroid carcinoma. Our group has also successfully used this therapy in similar clinical circumstances.

A 77-year-old man presented with recurrent hypercalcaemia (corrected serum calcium 2.73 mmol/l, normal 2.2–2.6) and a raised serum parathyroid hormone (PTH) of 16 pmol/l (normal 1.1–6.9), consistent with disease recurrence, 2 years after excision of a malignant parathyroid lesion. There was no evidence, either by ultrasound or nuclear medicine imaging, of recurrent disease in the neck, but CT scanning showed a right paratracheal nodule and three discrete lung nodules in keeping with pulmonary metastases. In the following 3 months, the hypercalcaemia deteriorated (peak corrected calcium 3.35 mmol/l requiring hospital admission for control of symptoms), but there was little response to cinacalcet or repeated infusions of bisphosphonates. Denosumab 120 mg was commenced and continued monthly. Within 4 days the corrected serum calcium had fallen from 3.14 to 2.74 mmol/l and has remained at this level for 4 months without recourse to hospital admission.

A 48-year-old man developed recurrent hyperparathyroidism (corrected serum calcium 4.22 mmol/l, serum PTH 145 pmol/l) 2 years after excision of a large, invasive parathyroid carcinoma followed by adjunctive external beam neck radiotherapy. He had previously undergone resection of an ossifying fibroma of the maxilla, and genetic analysis was in keeping with a diagnosis of hyperparathyroidism jaw tumour syndrome. There was no evidence of disease recurrence in the neck, but nuclear medicine and magnetic resonance imaging revealed uptake of sestaMIBI into a soft tissue osseous-based lesion in the T8 vertebra. Hypercalcaemia was refractory to fluid resuscitation, high-dose bisphosphonates and cinacalcet, so he was treated with a single dose of denosumab 120 mg. Within a week, the corrected serum calcium level fell to 2.46 mmol/l and he underwent resection of what, at present, appears to be a solitary skeletal metastasis. He remained well and required a low dose of alfalcacidol to maintain normocalcaemia.

As Karuppiah et al. (1) point out in their report, patients with parathyroid carcinoma rarely succumb to ‘cancer cachexia’ but, historically, have died of the complications of hypercalcaemia (2). Against this background, the known (albeit modest) risk of complications of repeated high-dose bisphosphonate infusions makes the emerging efficacy of denosumab in this clinical situation an important additional therapeutic option (3, 4). Formal clinical studies in this area are improbable, so evidence has to be accumulated from anecdotal reports (1, 4, 5). Our purpose here is to add to the published world experience and, accepting the paucity of long-term data, endorse its availability as a potential option for the treatment of refractory hypercalcaemia in this challenging disease.

Declaration of interest
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References


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